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OCTOBER 1952
VOLUME 48 NUMBER 4

Published Monthly by
AMERICAN MEDICAL ASSOCIATION
535 NORTH DEARBORN STREET • CHICAGO 10, ILLINOIS

Entered as Second Class Matter Feb. 7, 1929, at the Postoffice at Chicago, Under the Act of March 3, 1879. Annual Subscription, $12.00

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Since it is almost impossible to slab off less than one prism diopter, we suggest that when the error is less than one prism diopter one of the methods to be given in the December and February issues be used.

"IF IT'S A LENS PROBLEM, LET'S LOOK AT IT TOGETHER"

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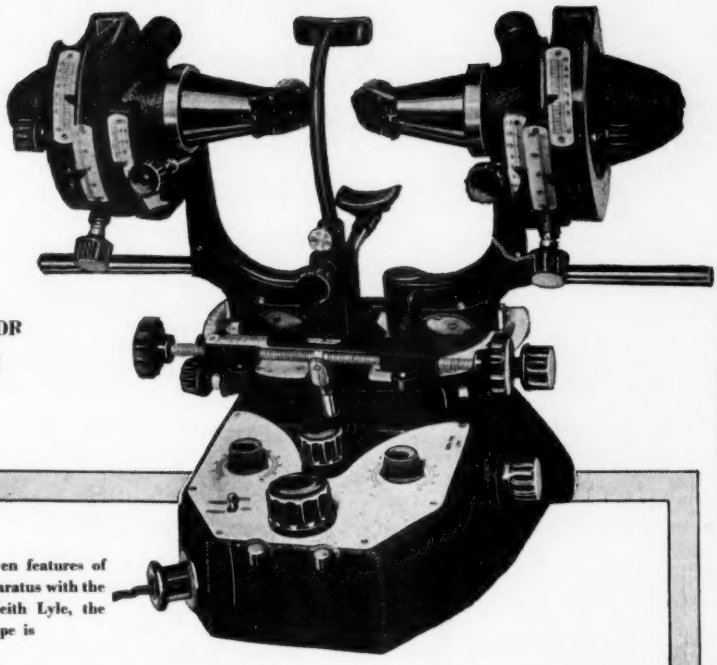

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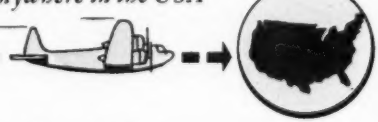

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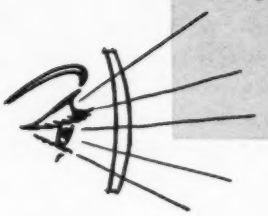

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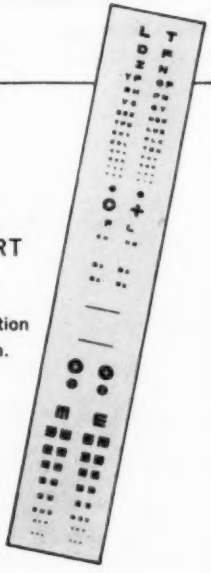

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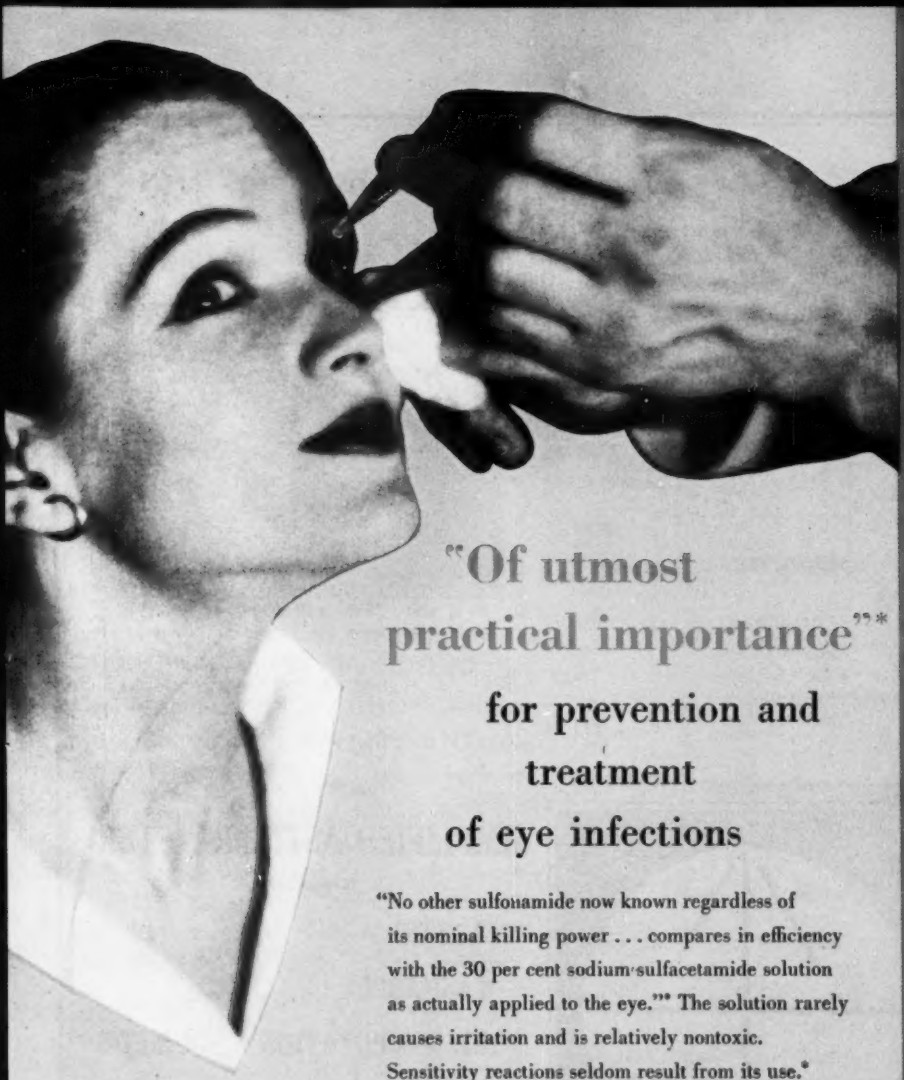

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*Kuhn, H.S.: Tr. Am. Acad. Ophth., p. 432, (March-April) 1951.

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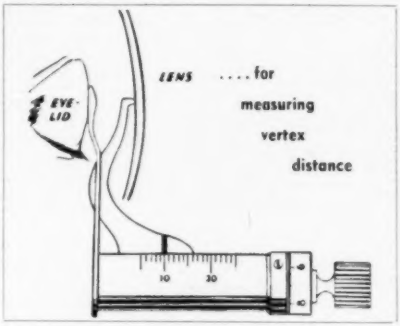

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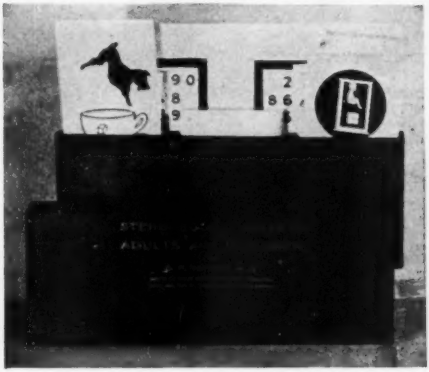

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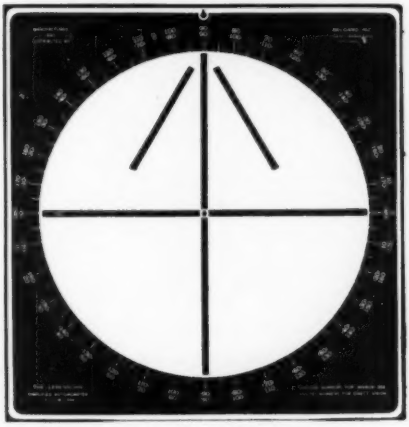

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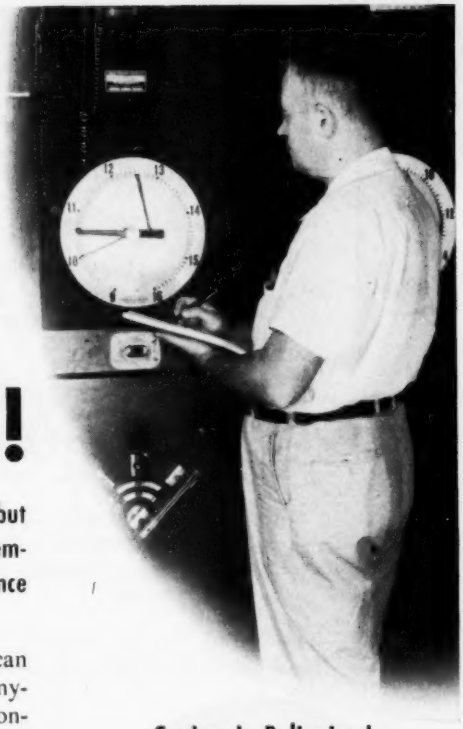

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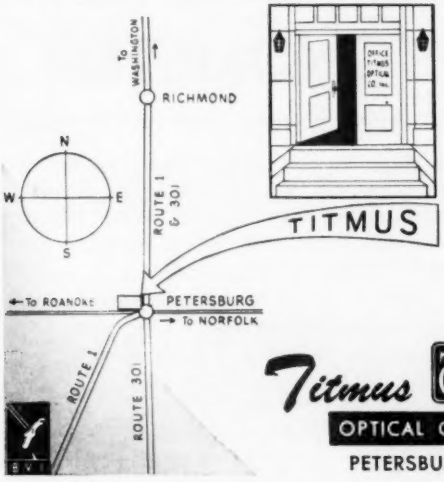

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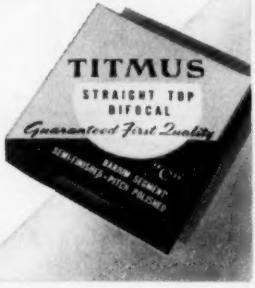

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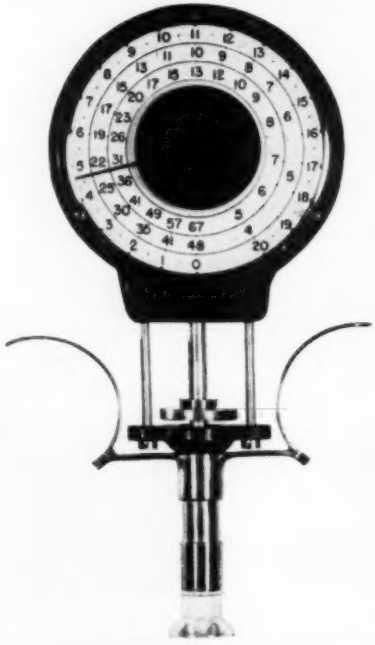

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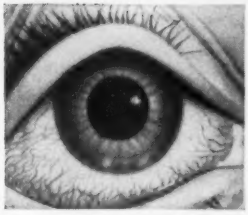

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1. Scheie, H. G., Tyner, G. S., Buesseler, J. A., and Alfano, J. E., *J. A. M. A. Arch. Ophth.* 45:301, March 1951.
2. Leopold, I. H., Purnell, J. E., Cannon, E. J., Steinmetz, C. G., and McDonald, P. R., *Am. J. Ophth.* 34:361, March 1951.

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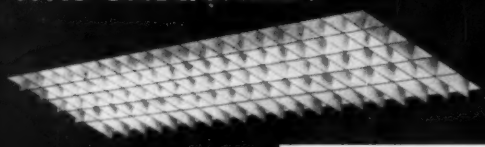

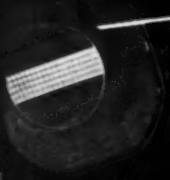

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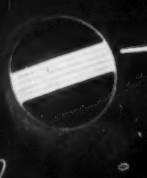
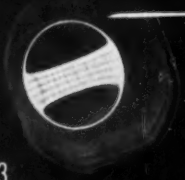


2

2 ... same polish, same curve, but exposed to 100° F *higher heat*. Note flux at lip of interface, and some distortion!



3

3 ... same polish, same curve, but exposed to 100° F *still more heat*. Note distortion throughout reading area! (Some bifocal makers use still higher heat.)

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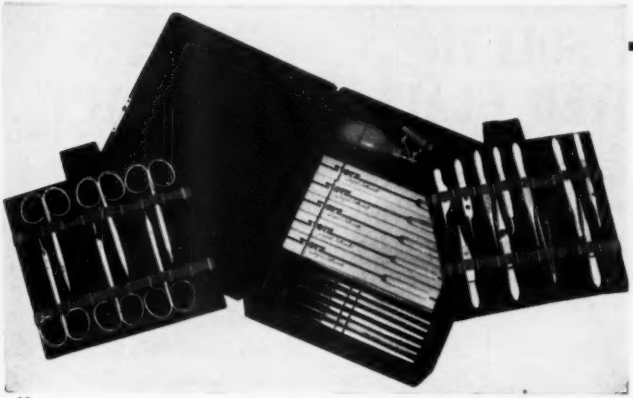

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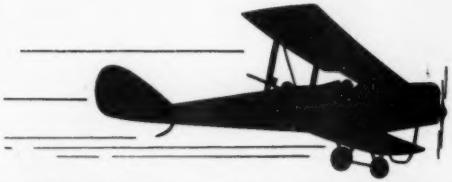

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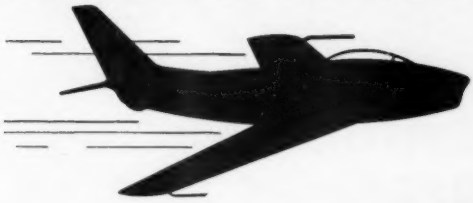

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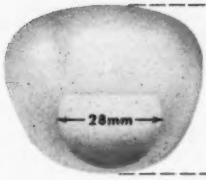

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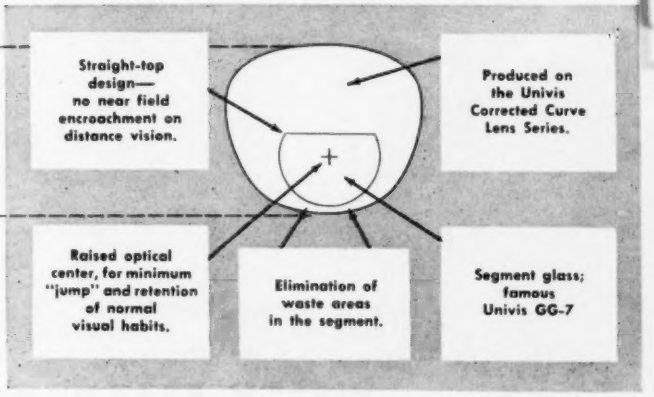
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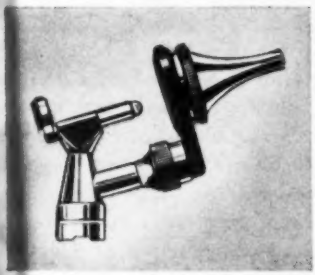

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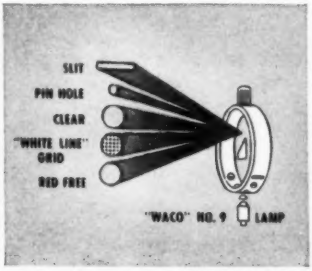

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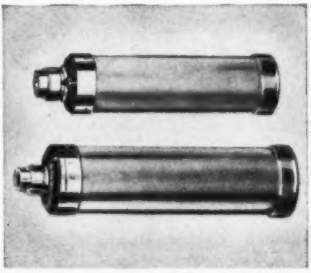

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VOLUME 48 OCTOBER 1952 NUMBER 4

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TONOGRAPHY

PETER C. KRONFELD, M.D.
CHICAGO

TONOGRAPHY is a new term for a procedure which consists essentially of the observation of the drop in ocular tension that occurs during prolonged or sustained corneal application of a tonometer of the Schiøtz type. Fundamentally, this drop in ocular tension is an example of the reaction of the normal human eye to localized pressure from without, causing deformation, indentation, and distention of the eyeball wall. At present tonography may be described as a promising approach to a number of ophthalmological problems, the unexplored ground vastly exceeding the explored territory.

HISTORY OF TONOGRAPHY

While the phenomenon of a drop in ocular tension under the influence of repeated or prolonged application of the tonometer was known to Schiøtz and his early followers, its first systematic study appears to have been made and reported by Wegner.[1] When a Schiøtz tonometer with the 5.5 gm. load was allowed to rest on the cornea of a normal eye for five to six minutes, it was found to cause a drop in ocular tension of at least one-third, and often one-half, the initial value. From measurements of the depth of the anterior chamber before and immediately after the application of the tonometer and from observation of the eyeground in blond persons, Wegner concluded that the drop in ocular tension was primarily due to displacement of blood from the uveal vascular system. He also made the observation—which is now the center of interest—that the drop in tension was of lower magnitude in glaucomatous than in normal eyes. During the decade following Wegner's publication this phenomenon received a good deal of attention. Bailliart,[2] in a lecture on tonometry before the Ophthalmological Society of the United Kingdom, referred to it as follows:

> Most frequently the tension falls after tonometric application. This fall of the tension is certainly comparable to the one described by many authors after the prolonged application of my dynamometer. But the reaction I have in view now is different because it is immediate. The needle has scarcely pointed to a figure than it goes down, sometimes by several divisions under that figure. . . . It scarcely takes the needle half a minute to accomplish this movement after which the needle will stop or only go down very slowly. This kind of reaction to tonometric application is by far the most frequent. It is a normal and consequently favourable reaction. It proves that the eye accommodates itself to a new pressure. It comes probably from a modification of the choroidal vascular system that allows itself to be flattened; it is one of its physiological properties to act as a pad regulating intra-ocular pressure.

Delivered as the Fourteenth de Schweinitz Memorial Lecture before the College of Physicians, Philadelphia, Section on Ophthalmology, Nov. 15, 1951.

1. Wegner, W.: Massagewirkung und Stauungsversuche am normalen und glaukomatösen Auge, Ztschr. Augenh. **55**:381, 1925.

2. Bailliart, P.: On Tonometry, Tr. Ophth. Soc. U. Kingdom **51**:412, 1931.

In some eyes Bailliart found the tension to remain stationary on application of the tonometer.

This phenomenon occurs with eyes appearing perfectly normal; it occurs too in severe forms of glaucoma. We can, to explain it, suppose that the choroidal pad has lost its normal elasticity, or that the (venous) blood-pressure is abnormally high while in the average eye it is scarcely higher than the ocular pressure, or that there is an obstacle to the venous circulation. This deals with cases in which the prognosis is less favourable.

In 1934 Boeck, Stough, and I [3] reported a statistical study of the drop in ocular tension that occurred in 100 nonglaucomatous eyes under the influence of a tonometer load of 15 gm. applied for two minutes. This amount of external pressure had been used before by Seidel [4] for the study of outflow phenomena from the human eye. Under this load, Boeck, Stough, and I found that the tension of nonglaucomatous eyes dropped 5 to 17 mm. The drop was greater in the eyes with initially higher tension. Glaucomatous eyes with initial tensions between 27 and 36 mm. showed a smaller drop than the nonglaucomatous eyes. In both series of cases the drop seemed fairly consistent and reproducible.

During the subsequent 15 years the response of the human eye to external pressure continued to be a subject of interest to a number of investigators, most notably Kukan, Perez Llorca, Diaz Dominguez, Bulson, Thomassen,[5] and a group of Russian authors. The dynamometer of Bailliart served as the test tool in a good part of these investigations. The differences in mechanism between dynamometry and tonography are probably only quantitative, and the results of the two testing procedures could be expected, and have actually proved, to be similar. To me, tonography appears to be the procedure in which the stimulus, that is, the artificial rise in intraocular pressure, is more accurately known and controlled than in dynamometry. Because of the dearth, at this time, of actual tonographic data, an exact comparison should probably not be attempted until a later date.

While not all pertinent publications have been available to me, it appears that Russion authors have made important contributions to the development of tonography. Dashevsky,[6] the principal worker in this field, recognized the rate of fall in ocular tension during continuous application of the elastotonometer to represent the rate of expulsion of fluid from the eye. The study of this rate of fluid expulsion proved useful in the early diagnosis, differential diagnosis, and therapy of the glaucomas.

Tonography received its name and new impetus about two years ago, largely as a result of three factors: (1) a clearer understanding of the relation between intraocular pressure and volume of the ocular contents, as an outgrowth of Friedenwald's theoretical analysis and physical measurements; (2) the arrival of a new tonometer that permitted more accurate measurements of the depth of the corneal

3. Boeck, J.; Kronfeld, P. C., and Stough, J. T.: Effect on Intraocular Tension of Corneal Massage with the Tonometer of Schiøtz, Arch. Ophth. **11**:796, 1934.

4. Seidel, E.: Zur Methodik der klinischen Glaukomforschung, von Graefes Arch. Ophth. **119**:15, 1927; Ber. Versamml. deutsch. ophth. Gesellsch. **46**:43, 1927.

5. Thomassen, T. L.: Experimental Investigations into the Conditions of Tension in Normal Eyes and in Simple Glaucoma, Particularly Performed by Subjecting the Eyes to Weight Compressions, Acta ophth., Supp. 27, 1946.

6. Dashevsky, A. I.: Tonometric Expression Testing and Its Clinical Significance in Glaucoma and Traumatic Ocular Hypotony, Vestnik oftal. **23**:21, 1944; abstracted, Am. J. Ophth. **29**:116, 1946.

indentation; (3) the increasing amount of evidence pointing in the direction of a steady flow of aqueous through the chambers of the eye and the effect of this evidence on prevailing concepts concerning the fluid exchange of the human eye. The principal workers in this field have been Moses and Bruno,[7] Grant,[8] Shahan,[9] Knighton, and deRoetth.[10]

PRINCIPLE OF TONOGRAPHY

The application of a tonometer of the Schiøtz type causes a change in the shape of the eyeball, consisting at first of a flattening of the part of the cornea that comes in contact with the footplate of the tonometer, plus a localized indentation of the cornea, due to the impingement of the plunger. Both processes, the flattening of the more peripheral, and the indentation of the more central, portion of the cornea, cause displacement of intraocular fluid, for which new space is found by distention of the eyeball wall to a degree somewhat greater than just prior to the application of the tonometer. The relative resistance of the eyeball wall to distention causes a rise in intraocular pressure. Impression tonometry, thus, entails a change in the shape of the eyeball, a movement or shift of fluid away from the impinging parts of the tonometer, and a rise in intraocular pressure.

As the tonometer remains on the cornea, one observes a steady rise in the tonometric reading, indicative of a corresponding increase in the depth of the indentation. This could be due to loss of ocular contents or progressive stretching of the eyeball wall. The latter possibility appears most unlikely from what is known about the limited distensibility of the eyeball wall. The inescapable conclusion, therefore, is that during prolonged application of the tonometer ocular fluids are expelled from the eye. The measurement of the rate of this fluid expulsion is the principal aim of tonography.

The interpretation of tonographic data requires an understanding of the quantitative relationships of physical and physiological factors concerned in the procedure. The physical factors are the change in shape of the eyeball, the amount of resultant fluid displacement, and the resultant rise in intraocular pressure.

The change in shape of the eyeball and the amount of resultant fluid displacement are partly measurable and partly calculable. The fluid displacement due to the change in shape of the cornea was determined experimentally by Friedenwald.[11] The results were published first as "volume displaced" in Table 1 of the paper by Moses and Bruno,[7] which shows the amounts of fluid displacement for the four commonly used tonometric loads and for the range from 0 to 20 scale units. These

7. Moses, R. A., and Bruno, M.: Rate of Outflow of Fluid from the Eye Under Increased Pressure, Am. J. Ophth. **33**:389, 1950.

8. Grant, W. M.: (*a*) Tonographic Method for Measuring the Facility and Rate of Aqueous Flow in Human Eyes, Arch. Ophth. **44**:204, 1950; (*b*) Clinical Measurements of Aqueous Outflow, A. M. A. Arch. Ophth. **46**:113, 1951; (*c*) Clinical Tonography, Tr. Am. Acad. Ophth. **56**:774, 1951.

9. Shahan, P. T.: Tonography: Studies of Aqueous Expulsion in Normal and Glaucomatous Eyes, to be published.

10. deRoetth, A., in discussion on Grant,[8b] p. 130.

11. Friedenwald, J. S.: Problems in the Calibration of Tonometers, Am. J. Ophth. **31**:941, 1948.

estimates of the amounts of fluid displaced could be refined further by considering the radius of corneal curvature of the eye in question (Friedenwald [12]).

Another set of values for the change in the shape of the eyeball as the result of tonometry was published by Grant. Using measurements and formulae developed by Friedenwald,[13] Grant obtained mathematical expressions for the total change in shape of the eyeball due to the application of the tonometer, that is, the flattening of the peripheral plus the indentation of the central portion of the cornea, plus the distention of the entire eyeball wall. Since during prolonged application of the tonometer the shape of the eyeball changes continually, and since tonography aims at the measurement of this change in the shape of the eyeball, Grant arranged the figures appearing in Table 1 of his first publication [8a] so as to express the change in ocular volume for a given tonometric scale reading with reference to a scale reading of zero, assuming that this change had been brought about by prolonged tonometry. The change in shape of the eyeball due to a tonometric load producing a reading of zero was arbitrarily set at zero. Grant's table, in other words, is designed specifically for the computation of tonographic results. For example, the figure of 20.1 cu. mm., which corresponds to a scale reading of 8 with a tonometric load of 10 gm., indicates that 20.1 cu. mm. of intraocular fluid is expressed from the eye if during a certain tonographic study the tonometric reading rises from an initial value of 0 to a final value of 8. If, in another instance, the tonometric reading with the 10-gm. weight rises from an initial value of 4 to a final value of 8, 20.1 —9.6 cu. mm., or 10.5 cu. mm., of intraocular fluid is expelled from the eye. In that tonographic sense, Grant's figures represent "volume changes for individual tonometer weights and individual scale readings." It should be realized that a short application of the tonometer changes the ocular shape but not the ocular volume. During prolonged application, however, the ocular volume undergoes a continuous change; the figures in Grant's table, as well as Friedenwald's values for the fluid displaced, represent estimates of this change in ocular contents, that is, of the amount of fluid expelled during tonography. Since there is almost a linear relationship between the two sets of data (Grant's and Friedenwald's), it seems irrelevant at this point which of these sets is used for the computation of results. For the reason that more of the data published thus far have been calculated on the basis of Grant's table, that procedure is being followed throughout this paper.

The other physical variable during tonography is the intraocular pressure. The rise in pressure involved in this procedure can be demonstrated and measured by applying the tonometer to the cornea of an eye the vitreous chamber of which is connected with a water manometer. This is the setup used in the process of calibration of tonometers, that is, in the process of determining the intraocular-pressure equivalents of the tonometric readings. The rise in intraocular pressure produced by the application of the tonometer is expressed in the symbols P_0 and P_T, the former signifying the pressure before,[14] and the latter signifying the pressure during,

12. Friedenwald, J. S.: Personal communication to the author.

13. Friedenwald, J. S., in discussion on Grant,[8b] p. 124.

14. The conversion tables supplied by the manufacturers of tonometers contain only P_0 values, since the clinician, ordinarily, is interested in knowing what the ocular tension was just before, and not during, the tonometric procedure.

the application of the tonometer. Systematic P_T measurements over the entire clinically important range of P_O values and for all four tonometric loads were made by a number of investigators, notably by Schiøtz and Friedenwald. The latter's findings were also first published in the paper by Moses and Bruno.[7]

Chart 1 shows the relationship between P_O and P_T for the 5.5-gm. load and for the range from 0 to 20 tonometric scale units as measured by Friedenwald. The ratio P_T/P_O can be seen to vary directly with the tonometric reading, that is, with the depth of the indentation produced by the tonometer. Also shown in Chart 1 is the relation between the tonometric reading and the change in ocular volume according to Grant.

As the result of the continued application of the tonometer, the normal human eye undergoes a change of some of its physical characteristics in the direction from a lower to a higher tonometric reading, that is, from the left to right of Chart 1. It is

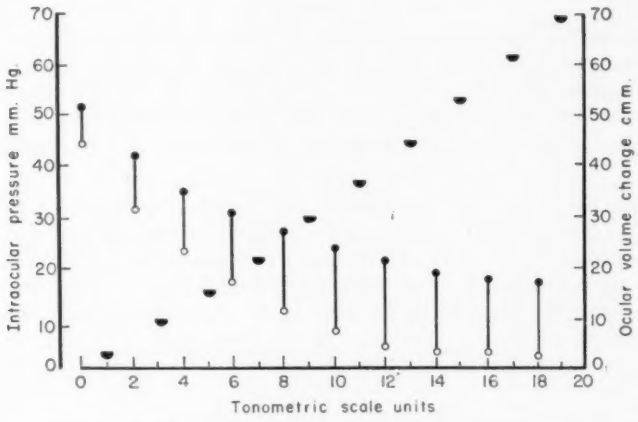

Chart 1.—Relationship between the ocular-volume change, after Grant (spherical segments), and the intraocular-pressure change, after Friedenwald (P_O, empty circles, to P_T, solid circles), caused by the application of the tonometer.

logical to consider the rise in intraocular pressure from P_O to P_T as the driving force that causes the expulsion of intraocular fluid. With the expulsion of fluid, the intraocular pressure drops; the eyeball wall becomes less distended, and the tonometric indentation increases in depth and volume. The increase in volume, ΔV, of the indentation alone (after Moses and Bruno), or augmented by the decrease in distention of the eyeball wall (after Grant), is a measure of the amount of fluid expelled from the eye during tonography. The tonographic result denotes, in principle, a loss in ocular fluid content under the influence of an artificially produced rise in intraocular pressure. In addition to these largely physical factors, physiological processes, such as changes in the rate of fluid production and in the intraocular blood volume, may play a part in tonography.

The nature of the fluid expelled is not entirely certain. Strong evidence in favor of expulsion of aqueous during tonography has been adduced by Grant. Observations on the flow in aqueous veins during the application of external pressure in

man (Goldmann [15]) or during injections of fluid into the anterior chamber in rabbits (Weekers and Prijot,[16] Greaves and Perkins [17]) lend further support to the view that the drop in tensions during tonography is primarily due to accelerated outflow of aqueous.

None of the observations thus far recorded rule out the possibility of a diminution in the total blood content of the eye during tonography. It would therefore seem inadvisable, at this early point, completely to lose sight of this possibility, but it does appear justifiable to state that the steady rise in tonometric reading during tonography indicates a corresponding decrease in ocular fluid, probably aqueous, content.

The results of tonography may be expressed graphically by plotting the change in ocular volume against time, or mathematically as the rate of fluid loss per millimeter of P_T. Moses and Bruno calculated this volume-pressure ratio in accordance with the formula

$$\frac{\Delta V}{\text{Average } P_T \times \text{time}}$$

ΔV is obtained by looking up in Friedenwald's table [18] the volume displaced for the initial and final tonometric readings and deducting the former from the latter. From the same table, the P_T values for the initial and for the final tonometric reading are obtained and their arithmetic mean determined (average P_T).

Grant expresses the result of tonography in accordance with the formula

$$\frac{\Delta V}{(\text{Average } P_T\text{-}P_O) \times \text{time}}$$

He obtains the ocular-volume equivalents of the initial and final tonometric readings from his Table 1.[8a] The average P_T-P_O is computed as the arithmetic average of the pressure increment, P_T-P_O, for successive half-minute intervals. Practically the same result is obtained by determining the arithmetic mean of the initial and the final P_T and deducting from it P_O, which is the intraocular pressure immediately before the tonography. For the final result, which, again, is a volume-pressure ratio, Grant has introduced the term "coefficient of facility of outflow" (C).

TECHNIQUE OF TONOGRAPHY

The technique of tonography is essentially that of tonometry. The examinee is placed in a supine position on a comfortable couch or examining table, with enough support of his head and removal of clothing around his neck to insure unimpeded venous flow from the head to the heart. The significance of this factor was demonstrated by Shahan. It is advisable to include a pretest period of from 20 to 30 minutes, during which three to four tonometric readings are taken, in order to ascertain the prevailing phase of P_O, steady, rising, or falling. The optional length of the test period itself appears to be between four and six minutes.

The essential equipment consists of an electronic tonometer, such as that manufactured by V. Mueller & Co. It has two advantages over the regular Schiøtz

15. Goldmann, H.: Studien über den Abflussdruck des Kammerwassers beim Menschen, Ophthalmologica **114**:81, 1947.

16. Weekers, R., and Prijot, E.: Recherches expérimentales sur les fonctions des veines aqueuses, Ophthalmologica **119**:321, 1950.

17. Greaves, D. P., and Perkins, E. S.: Aqueous Veins in Rabbits, Brit. J. Ophth. **35**:119, 1951.

18. Moses and Bruno,[7] p. 390.

instrument: greater accuracy of the individual reading, and easier, almost effortless, maintenance on the examinee's cornea. A recording galvanometer is a great convenience, but not absolutely essential. A staff of two persons is necessary, one to watch and reassure the patient and, at the same time, to keep the tonometer head in proper position, and another to take and record the readings. It is often convenient to have a third person to "run interference," that is, to keep out potentially disturbing elements. Of the factors that influence tonography, a great many must be assumed as being still unknown. Unsteadiness of fixation, obviously, is a very disturbing factor. It is important therefore to carry out the tonographic procedure in a quiet room without any "excuse" for ocular movements on the part of the patient. Slight unsteadiness of the lid, i. e., incomplete lid-closure movements, are usually not disturbing.

The actual procedure of tonography entails no subjective discomfort of any kind, to which fact I can testify from my own experience. The use of the local anesthetic

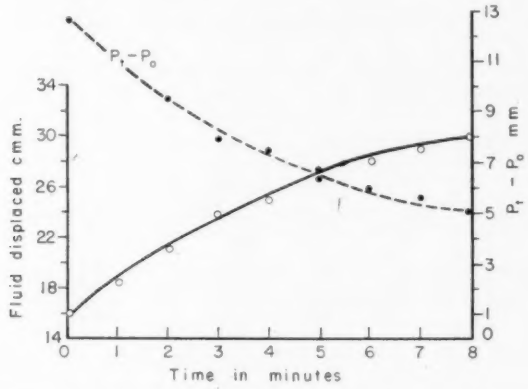

Chart 2.—A typical tonogram of a nonglaucomatous human eye (solid line).

in both eyes entails a slight blurring of vision for about an hour. A slight foreign-body sensation of about three hours' duration may follow the procedure. I know of no instance of any complication attributable to tonography.

THE TYPICAL TONOGRAM

The tonograms of undiseased eyes reported more or less summarily by Moses and Bruno, Grant, and Shahan seem to be in good agreement with regard to the general character of the tonographic curve and its individual variations. My experience with undiseased eyes has been as follows:

Tonometric readings taken every 15 seconds and converted into cubic millimeters of volume change (after Grant) in more than one-half the grossly undisturbed tests make a curve of slowly decreasing slope (Chart 2). This gradual tapering off seems to be related to the gradual diminution of P_T during the tonography, since the coefficient of outflow for the four consecutive two-minute periods of Figure 2 is fairly constant, namely, 0.23, 0.24, 0.22, and 0.22. Similar results were obtained for three

consecutive two-minute periods for the six patients listed in Table 1. These observations support Grant's concept of a direct proportionality between pressure increment and fluid displacement within the P_T range produced by a given tonometric load in a given eye. For the considerably wider P_T range produced by loads varying from 5.5 to 15 gm., my findings point more toward a direct proportionality between ΔV and the average P_T, so that the latter may prove to be a more practical denominator for the expression of tonographic results than the average $P_T - P_O$. Since the majority of the tonographic data published thus far has been expressed in terms of Grant's coefficient, his procedure has been followed throughout this paper.

TABLE 1.—*Tonograms of Six Nonglaucomatous Eyes with Early Cataract Broken Down into Three Consecutive Two-Minute Periods and Expressed in Terms of Coefficient of Outflow: C_1, C_2, C_3*

Patient	C_1	C_2	C_3
R. N.	0.38	0.35	0.39
E. D.	0.63	0.69	0.66
N. M.	0.23	0.24	0.19
J. B.	0.36	0.37	0.36
J. B.	0.54	0.60	0.61
N. N.	0.20	0.20	0.21

TABLE 2.—*Six Tonograms of the Right Eye, with Early Cataract, of W. N., Aged 58* *

Test No.	Po	Change in Ocular Volume, Cu. Mm. After (Minutes)						Coefficient of Outflow
		Initial	1	2	3	4	5	
1	11	28.1	33.7	35.5	40.0	42.0	45.3	0.28
2	11	27.0	33.7	36.6	39.2	43.2	45.3	0.24
3	13	25.6	30.5	34.4	39.2	41.6	43.2	0.25
4	12	27.0	32.8	40.4	39.2	43.6	44.5	0.26
5	12	27.0	32.0	35.5	41.2	44.5	45.3	0.29
6	13	25.3	32.8	35.5	37.3	41.6	45.3	0.29
								Mean 0.267 Variations observed ± 10%

* The tests were done on consecutive days during midmorning hours.

In a little less than 50% of the undiseased eyes which I have tested, the tonographic curve deviated from a smooth one in that two to three times during the four minutes of tonography the ascending curve was interrupted by a plateau, or even a slight recession, lasting 30 to 45 seconds, at the end of which period the curve became ascending again. Since this phenomenon was noticeable in tonograms showing the ocular pulse, it is highly probable that the plateaus were not due to friction within the tonometer head but indicated a real discontinuity in the process of fluid loss. Whether short phases of increased fluid formation or of decreased outflow are responsible for these plateaus will be dealt with specifically in a subsequent publication. These irregularities are usually so slight that a gradually tapering-off curve can easily be fitted to the readings obtained every 15 seconds.

I have been particularly interested in the test-retest consistency of tonographic measurements repeated on the same eye under consistent external conditions. A typical example of such a study is shown in Table 2. The tonograms listed there were obtained from the right, early-cataractous eye of a 58-year-old white man who,

for the purpose of this study, was admitted to the hospital with "up-and-around" privileges. After a two-day period of indoctrination and adjustment, and without any medication other than the instillations of a sulfonamide drug, tonographic tests were done daily between 10 and 11 a. m. Table 2 reveals a consistency of the coefficient of outflow within the limits of ± 10% of the arithmetic mean. Undiseased eyes of outpatients tested at different times of the day yield a coefficient of outflow consistent within ± 25% of the arithmetic mean. Moses and Bruno reported a range of ± 30%, and Grant a slightly narrower range, for the variations occurring in the same undiseased eye. To what extent these variations are real, that is, due to differences in the response of the same eye to the same stimulus, or accidental, that is, due to imperfections of the technique of tonography, I find impossible to decide at this point. There already exists evidence that the response of the same eye to the same tonometric load varies physiologically. The variations associated with the estrous cycle (Shahan [9]) are probably the most striking example. I have observed a fairly consistent difference between forenoon and afternoon tonographic readings on the same eye, the latter usually yielding a higher coefficient of outflow. It is to

TABLE 3.—*Distribution of Undiseased Eyes and Eyes with Early Glaucomas over Range of Coefficients of Outflow Thus Far Observed (Kronfeld)*

	Coefficient of Outflow								
	0-0.049	0.050-0.099	0.100-0.149	0.150-0.199	0.200-0.249	0.250-0.299	0.300-0.349	0.350-0.399	0.4-0.599
40 undiseased eyes.....	..	..	2	12	8	9	6	2	1
34 eyes with early glaucoma..	6	12	10	6	..	..	..	..	..

be hoped that more of the physiological factors influencing the tonogram will become known in the near future. Until then, caution should be exercised in interpreting single tonograms.

The tonograms of undiseased eyes of different subjects vary within much wider limits than repeated tonograms on the same eye. Grant has reported a range of 0.11 to 0.44, with an average of 0.22. My findings in 40 nonglaucomatous eyes, eyes with early cataract, or undiseased eyes indicate a range of from 0.14 to 0.44, with an average of 0.24. Each of these eyes was tested at least three times and possessed close to average ocular rigidity. A close comparison with the findings of Moses and Bruno and Shahan will not be attempted here because they would require conversion into coefficients of facility of outflow, entailing considerable inaccuracies. The close agreement between the findings of Grant and my own is remarkable and strongly suggests their representativeness. Since tonography is expected to serve as a means of distinguishing between glaucomatous and nonglaucomatous eyes, the establishment of a lower border of normal is highly desirable. With the exception of the atypical response described in the following series, I have not encountered a nonglaucomatous eye which on repeated examinations revealed an average coefficient of outflow of less than 0.14. The occurrence of such eyes has, however, to be expected, from the massing of undiseased eyes in my group of outflow coefficients of between 0.150 and 0.199 (Table 3) and from deRoetth's finding of coefficients of outflow below 0.15 in 9 of 100 nonglaucomatous eyes.

In a number of undiseased human eyes, characterized by an unusually low ocular tension,[19] I observed an atypical behavior during the tonographic procedure. Instead of the steady increase in tonometric reading described as the typical tonogram in the foregoing section, the reading remained constant or described up-and-down fluctuations, without any upward trend, for one, two, or all five minutes of the tonographic test. The phenomenon was observed three or four times in more than 20 undiseased eyes. Some of these eyes gave a normal tonographic response at other times, usually when their ocular-tension reading was somewhat higher. The phenomenon seemed significant enough to warrant study with lighter tonometer and plunger loads; such studies are now in progress and will be reported at a later date. A graphic recording of the tonographic data clearly characterizes these eyes as atypical. Their unusually low initial ocular tensions distinguish them from glaucomatous eyes. Another distinguishing feature is the striking drop in tension, which starts immediately after the removal of the tonometer and becomes most marked two minutes later.

Returning to the typical behavior of undiseased eyes, the range of 0.11 to 0.44 reported by Grant or of 0.14 to 0.56 reported by me seems to be real; that is, it seems to represent true individual differences in the response to the tonometric pressure not related to the magnitude of the stimulus or to the initial tension, both of which varied but slightly in these populations. The method of treatment of the data, that is, the calculation of the coefficient of outflow, should have eliminated any possible effect of these slight differences in initial tension. No other logical treatment of the data caused a reduction in the magnitude of the individual variations.[20] It is therefore probable that they represent true individual variations.

TONOGRAM OF THE GLAUCOMATOUS EYE

Low coefficients of outflow in eyes affected with chronic glaucoma have been reported by Moses and Bruno, Grant, Shahan, Knighton, and deRoetth. The consistency of these findings establishes and reaffirms impaired outflow of fluid under external pressure as a characteristic of chronic glaucoma. It is only natural that this finding has given rise to extensive investigations into the diagnostic possibilities of tonography. In the application of tonography for diagnostic purposes, it becomes important to consider carefully all preexistent differences between the undiseased and the glaucomatous eye and to adjust the tonometric stimulus so as to compensate for any such differences. By expressing the result of tonography as ΔV divided by P_T, one may safely assume that the possible effect of differences in original tension has been eliminated as long as one is dealing with eyes in which ΔV is directly proportional to P_T. In the glaucomatous eyes, as will be shown in a later publication, the normal proportionality between P_T and ΔV may be absent. In a comparison of undiseased and glaucomatous eyes, the tonometric stimulus should, therefore, be adjusted to the same relative magnitude; in other words, in the light of the foregoing discussion, the increases in intraocular pressure produced by the application of the

19. These eyes were not included in the series of 40 eyes with early cataract or undiseased eyes which served to establish the normal range of coefficients of outflow.

20. Attention will be paid in the future to possible effects upon the coefficient of outflow of individual variations in corneal curvature which have been shown to have a definite effect upon the volume displaced (Friedenwald [11]).

tonometer should be of about the same relative magnitude. This requirement is met —with an accuracy that seems commensurate with the present status of tonography—by adjusting the tonometric load so that approximately equal depths of indentation are produced in undiseased and in glaucomatous eyes. The effect of this procedure is shown in Table 4 for the tonometric reading of 8 scale units. In terms of $P_T - P_O$, P_T/P_O, or of fluid displaced, the stimuli entailed in applying the 7.5-gm. load to an eye with P_O=20, and in applying the 10-gm. load to an eye with P_O=29 differ from each other by not more than 20%. Tonographic comparisons of nonglaucomatous and glaucomatous eyes may thus be considered "fair" as long as equal initial tonometric readings are obtained.

For such a comparison were used 34 eyes which met all of the following requirements: (1) repeated tonometric readings of between 28 and 35 mm. Hg Schiøtz; (2) close-to-average rigidity; (3) a positive water-drinking test, that is, a rise of ocular tension of 6 mm. or more, or a rise from an initial tension below 30 mm. Hg (Schiøtz) to a value above this level; (4) minimal or no demonstrable visual-field change; (5) wide, roomy chamber angles, and (6) no other significant signs of ocular disease.

TABLE 4.—*Intraocular Pressure and Ocular Volume Changes Produced by Two Different Tonometric Loads Causing Indentation of Equal Depth (8 Scale Units)*

P_O	Tonometric Load	P_T	P_T-P_O	P_T/P_O	Ocular Volume Change, Cmm.
20	7.5	36.5	16.5	1.82	22.9
29	10	48.7	19.7	1.68	20.1

Eyes meeting these requirements were considered to represent early stages or a mild form of chronic open-angle glaucoma. In several of the patients included in this study one eye was in an advanced stage of glaucoma.

The tonographic tests on these eyes with early glaucoma were done during late morning hours, with the patient enjoying outpatient status. All local or systemic forms of treatment for the glaucoma were discontinued one week prior to the test. Every eye was tested at least three times. The variations in the coefficient of outflow observed under these conditions did not exceed ± 25% of the arithmetic mean for any of the 34 eyes of this group. These means ranged from 0.026 to 0.182. If this range is divided into four subranges and each eye is listed within its respective subrange (Table 3), a fairly symmetrical distribution around the average of 0.099 of the coefficient of outflow for eyes with early glaucoma is revealed. Table 3 also shows the distribution of the coefficients of outflow for the group of undiseased eyes, referred to earlier. It can be seen that within the ranges of 0.100 to 0.199 the glaucomatous and the undiseased eyes overlap. Since chronic open-angle glaucoma most probably develops out of a state of normalcy, and since the coefficients of outflow vary considerably for undiseased eyes, a certain amount of overlap between eyes with early glaucoma and undiseased eyes had to be expected. The findings recorded in Table 3 indicate a decided difference in the facility of outflow of nonglaucomatous eyes and eyes with early glaucoma. The difference is of sufficient magnitude to be of diagnostic value in the majority of eyes with early glaucoma.

These findings appear to be in accord with those of practically all previous and present workers in this field.

The value of tonography can be demonstrated further by correlating the facility of outflow and the ocular tension at the beginning of the test (P_0). This has been done in Chart 3 for those instances in which the initial tension was below 30 mm. Hg. In a number of instances the tonographic result is more strongly suggestive of glaucoma than the ocular tension.

Aside from its established diagnostic significance, tonography promises to become a valuable tool in the study of the pathogenesis, as well as in the follow-up, of glaucomas. Work in that direction is now in progress at several institutions in the United States.

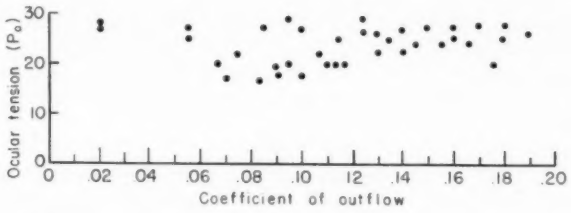

Chart 3.—Coefficients of facility of outflow of eyes with early glaucoma, determined when the initial ocular tension was below 30 mm. Hg (Schiøtz).

SUMMARY

Tonography is a recent refinement of an investigative technique that has been in use in ophthalmology for over 25 years. It consists, in principle, of the measurement of the drop in ocular tension that occurs during, and as the result of, an external, eyeball wall-indenting force. The response of the eyes with early, chronic, open-angle glaucoma differs characteristically from that of the undiseased eye. Tonography, therefore, is of great value in the early diagnosis of chronic glaucomas. Tonography may be expected to yield valuable information concerning the pathogenesis of glaucomas and related diseases.

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ZONULE MEMBRANE AND CATARACT EXPRESSION

DERRICK VAIL, M.D.
CHICAGO

IT IS A happy assignment to address one's colleagues in honor of Arthur J. Bedell, honorary surgeon of this famous, busy, and useful hospital, whose doors have been open now a few days more than 118 years. I am grateful for the opportunity to pay my respects to Dr. Bedell, whose lifelong devotion to ophthalmology has done so much to advance its interests, and whose scientific contributions, notably in the field of interpretive photography of the fundus oculi, have helped our patients and ourselves in times of difficult decision.

I have selected this subject because of the essential role that the zonule plays in modern intracapsular surgery. In spite of an extensive literature going back to the middle of the 18th century, not very much information about the zonule is at ready hand (however, see Beliner's "Biomicroscopy of the Living Eye" [1]) and available for practical application to the problem of removal of the cataractous lens in its capsule with minimal injury to the intraocular contents. Indeed, I could find but one major article in the literature. It is by Jacob Goldsmith,[2] and deals exclusively with this problem. It deserves the fullest study by all ophthalmic surgeons. Harrington [3] has also written on this subject. His papers are thoughtful discussions and worthy of attention. Much information on this topic can be found in Kirby's "Surgery of Cataract." [4]

DEVELOPMENT OF THE ZONULE

In the embryo, according to Mann [5] and Haden,[6] the earliest appearance of the zonule is at the 65-mm. or nine-week stage. The early zonular fibers can be seen to originate from the inner layer of the optic cup as processes from the ectodermal cells and to grow toward the lens surface. Studies of Merz and myself [7] lead us to

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Delivered as the Arthur J. Bedell Lecture at the Wills Hospital, Philadelphia, March 21, 1952.

1. Berliner, M. L.: Biomicroscopy of the Eye: Biomicroscopy of the Living Eye, Vol. 2, New York, Paul B. Hoeber, Inc., 1949, p. 1327.

2. Goldsmith, J.: Dynamics of Intracapsular Cataract Extraction, Arch. Ophth. **29**:380, 1943.

3. Harrington, D. O.: Mechanics of Intracapsular Cataract Extraction, Arch. Ophth. **42**:23, 1949; Dynamics of Phakoerisis, Am. J. Ophth. **34**:10, 1951.

4. Kirby, D. B.: Surgery of Cataract, Philadelphia, J. B. Lippincott Company, 1950, p. 425.

5. Mann, I.: Development of the Human Eye, London, Cambridge University Press, 1928.

6. Haden, H.: Certain Phases of the Development of the Vitreous, Tr. Am. Ophth. Soc. **48**:71, 1950.

7. Vail, D., and Merz, E. H.: Embryonic Intra-Epithelial Cyst of the Ciliary Processes, Tr. Am. Ophth. Soc. **49**:167, 1951.

agree with Mann and Haden, who believe that the zonule is entirely ectodermal in origin and develops from the inner layer of the optic cup, and is not a mesodermal structure, coming from the primary vitreous, as is held by others. Drualt's bundle, which is crossed at right angles by the zonular fibers, now begins to disappear. Is it possible that the remains of the primary vitreous forms the cement substance of the membrane, ensheathing the fibers? The rim of the cup is advanced forward on the surface of the lens and still approximates it. Ciliary processes are forming. The space between the two layers of the optic cup is still open.

At the 110-mm., or four-month, stage the zonular fibers can be seen to reach the lens. These fibers have formed definite anterior and posterior layers. The ciliary folds and ciliary body are well developed and are in close contact with the equator of the lens. The rudimentary iris is growing forward over, and in contact with, the anterior surface of the lens. The two layers of the optic cup have become approximated and the space between them obliterated. The zonular membranes, anterior and posterior, are relatively tough at this stage. In the fresh preparation one can notice how closely the ciliary processes approximate the lens. It is also noted at this time that the zonular fibers originate from the lateral surfaces of the ciliary processes and in the depth of the valleys.

By the fifth month, or 150-mm. stage, the zonular membrane seems to have fully developed and the marginal sinus of Szily is closed.

ANATOMY

As far back as 1723 François Pourfour de Petit injected air into the space between the zonule and the vitreous and described the canal that bears his name. In 1740 Antoine Maitre-Jan, *chirurgien du Roy a Méry-sur-Seine,* wrote [8]:

> I notice first that it (the lens) is situated in the middle of the anterior part of the vitreous body, vis-à-vis the uveal circle; that it is firmly retained in this place by the membrane of the vitreous body, which, as I have already said, divides into two membranes, one of which continues to surround the anterior part of the vitreous, and the other passes over the lens and embraces it with such strength that it cannot change its position.

In 1755 Abram Vandenhoeck, of Göttingen, printed a book, now scarce, "Descriptio anatomica oculi humani, iconibus illustrata," by Johann Gottfried Zinn. In it the author described the suspensory mechanism of the lens as a delicate membrane extending from the ciliary body back to the lens—whence the name zonule of Zinn.

Since then, many men famous in ophthalmology have described the zonular membrane as they saw it in the days before the development of histologic technique and as they have seen it since. The older anatomists, as Salzmann [9] called them, such as Maitre-Jan, Saint Yves, Winslow, Petit, Zinn, Dollinger, Iwanoff, and Schwalbe, regarded the zonule as a simple expansion of the anterior part of the hyaloid membrane. Merkel (1870) was the first to suggest that the fibers were united with each other by a cement (*Kittsubstanz*) into a sort of membrane. Beginning with Dessauer and Czermak, in 1885, and the histologic study of stained sections, the membranous nature of the zonule was lost sight of and its existence

8. Maitre-Jan, A.: Traité des maladies de l'œil, Paris, Breton, 1740, p. 40.

9. Salzmann, M.: The Zonula Ciliaris and Its Relation to Neighboring Structures, Translated by E. V. L. Brown, Ann. Ophth. **17**:1; 240, 1908.

even denied, for in the preparatory process of hardening the cement substance disappeared. Thus, even in the 1924 English edition of Fuchs's textbook[10] the following description of the zonula ciliaris is presented:

> The zonula ciliaris consists of delicate, homogeneous fibers, which take their origin from the inner surface of the ciliary body, beginning at the ora serrata. The fibers at first keep in contact with the surface of the ciliary body, but leave it at the apices of the ciliary processes, and, becoming free, pass over to the edge of the lens. . . . As they do this, they diverge so that some go toward the very equator of the lens, others in front of the equator and behind it, to reach the lens capsule, with which they become fused. The space, triangular on cross section, included between the fibers of the zonula and the equator of the lens, is called the canal of Petit [sic]. It is connected with the posterior chamber by means of slit-like gaps between the separate fibers of the zonula.

We see, then, that in this bible of ophthalmology two errors, the result of histologic studies, have been committed: the mistake of identifying Hannover's canal for that of Petit, and no mention of the cement substance.

Two years before this, Beauvieux,[11] unhappy over the conflicting views and opinions found in the voluminous literature of the subject, undertook the study of fresh specimens with the corneal microscope and slit lamp and described the zonula ciliaris as a continuous membrane on or in which run the zonular fibers, bound together by an interfibrillar or transparent substance. Two years later Egger,[12] using the same method of examination but also staining the tissue with Fleming's solution and Weigert's neuroglial and other stains, confirmed Beauvieux' findings. Since then Loddoni, Moreno, Teulières and Beauvieux, Duke-Elder,[13] Troncoso,[14] Goldsmith,[15] and Minsky[16] have made further important contributions. Vogt's beautiful "Atlas" should also be consulted.

In spite of a few unresolved controversial points, the modern conception of the zonular membrane is as follows:

The zonule is composed of a thin, pellucid membrane, not unlike cellophane,* in which course thin prismatic strands of glass-like fibers more or less systematically. The membrane is viscid and similar to vitreous. When viewed from behind, it is seen to arise at the ora serrata, and, sweeping forward, and filling every crevasse and contour of the pars plana (orbiculus ciliaris), it leaves and, traversing obliquely the perilenticular space, inserts into the posterior capsule of the lens about 0.2 mm. from the equator. When seen from in front, it appears to arise in the valleys and along the sides of the ciliary processes and, covering all but their heads or tips, extends toward the equator of the lens to begin its insertion 0.5 mm. from the

10. Fuchs, E.: Textbook of Ophthalmology, Ed. 8, revised, Philadelphia, J. B. Lippincott, 1924, p. 25.

11. Beauvieux, M. J.: The Zonule, Arch. opht. **39**:410-484, 1922.

12. Egger, A.: The Zonule of Zinn of Man According to the Investigation of the Cadaver Eye with Biomicroscopy, von Graefes Arch. Ophth. **113**:1, 1924.

13. Duke-Elder, W. S.: Text-Book of Ophthalmology, Vol. II, Henry Kimpton, London, 1932, p. 133.

14. Troncoso, M. U.: Microanatomy of the Eye with the Slitlamp Microscope: II. Comparative Anatomy of the Ciliary Body, Zonule and Related Structures in Mammalia, Am. J. Ophth. **25**:1, 1942.

15. Goldsmith, J.: Slitlamp Observations During Experimental Intracapsular Cataract Extraction, Arch. Ophth. **22**:792, 1939.

16. Minsky, H.: Concept of Zonular Chamber, Arch. Ophth. **28**:214, 1942.

equator. The perilenticular space enclosed by the membranes is Hannover's canal, in which are found, according to Goldsmith, Liesegang rings, presenting the character of colloids. Goldsmith further states [15]:

> Since Hannover's canal constitutes an afferent and efferent pathway for the nutrition of the lens, changes in the colloidal system of this canal may possibly be the true initiator of the formation of cataracts.

Histologically, the fibers are, according to Egger, about 6 to 7 mm. long, their thickness varying from 9 to 40 mm. After separation or rupture the fibers spring back toward the ciliary body. The fibers are more numerous in the embryonic life and in infancy, decreasing with age. They arise about 1 mm. from the ora serrata (some of them, however, still farther back, in the inner limiting membrane of the retina). Here they are thicker and more compressed. Most of them arise in the furrows of the ciliary processes and, except only occasionally, run forward, avoiding the crests of the ciliary processes. Otherwise they would interfere with the secretory epithelium. Sometimes they course over the crests "like a string over a violin bridge" (Beauvieux). They become less numerous in the region of the ciliary processes.

The fibers diverge in the direction of the equator. Some investigators consider that the fibers arising from the ora serrata cross at the bases of the ciliary processes with the fibers arising from the latter, to become inserted into the anterior capsule. The fibers which arise in the furrows or grooves of the ciliary processes are directed toward the posterior part of the lens to be inserted into the posterior capsule. Short fibers arise directly in the ciliary body to be inserted into the periphery of the lens, at the equator. Some of the fibers run more or less obliquely to bridge the valleys; others, and this statement is disputed, insert into the vitreous in the ora-serrata zone (Déjean, Landau [16a]). Some are inserted backward into the retina a little beyond the ora serrata. Others, and this view is also disputed, reach the anterior limiting layers of the vitreous and unite with the hyaloid membrane, forming the ligamentum hyaloideocapsulare of Wieger, a circle of condensation of the hyaloid fibers in the retrolental fossa, or space of Berger, attached to the posterior capsule of the lens. According to Berger, however, the internal layer of the zonule of Zinn has nothing to do with the hyaloid membrane, a belief in which Beauvieux and Goldsmith concur, but which is disputed by Krimsky and Redslob,[17] the latter of whom cites Koby as seeing fibers running back from the posterior lens capsule into the hyaloid membrane. In the embryo, however, connecting fibers have been noted.

Duke-Elder [13] believes that the "zonule, which is embryologically a specialized region of the vitreous, is secreted in a manner closely similar to this structure; instead of being formed from the retina itself, as is the vitreous, it is formed as an extra-cellular product of the ciliary epithelium—the prolongation of the retinal elements over the ciliary body." But however it is formed, the fact remains that its contact with the ciliary processes, pars plana, and ora serrata is evidently strong, and firm enough for lifetime work in accommodation. Krimsky's "hanging-vitreous" preparation is a testimony of its connection with the vitreous. His striking motion

16a. Landau, E.: Contribution to the Histology of the Eye, Ophthalmologica **112**:129, 1946.

17. Redslob, E., in Bailliart, P.; Coutela, C.; Redslob, E., and Velter, E.: Traité d'ophtalmologie, Masson & Cie, Paris, 1939, Vol. 1, p. 573.

picture of the lens-vitreous preparation demonstrates effectively that the isolated vitreous hangs fastened to the lens by means of the zonular membrane because of its attachment to the hyaloretinal line in the hyaloid membrane.

The insertion of the zonular membrane into the lens capsule at the equator is likewise a strong one. The nature of the cement substance that joins zonule and lens capsule together is entirely unknown, but it deserves careful study by modern biochemical methods. We know from practical experience that its tenacity varies with age and with the state of nutrition and of health or disease. The insertion in the anterior capsule begins 0.5 mm. from the equator and ends, perhaps irregularly, about 1.5 mm. farther forward. In the posterior part the zonule begins to insert about 0.2 mm., and ends about 0.8 mm., from the equator, so that the relation of front to back insertions is 3:2 (Duke-Elder). Its posterior border coincides almost exactly with the ligamentum hyaloideocapsulare. Occasionally, in examining a patient with a congenital coloboma of the iris by means of the biomicroscope, one can see the course of the glass-like fibers ending in brushes, to be inserted a surprisingly large distance into the anterior capsule.

The fibers and membranes, anterior and posterior, inserting into the lens capsule form the zonular lamella. Careful examination of lenses removed in their capsules shows no evidence of remaining zonular lamellae, fibers, or membrane. This is of the utmost practical importance, although Redslob believes that on extraction of the lens in its capsule the fibers (membrane) are "ruptured" in the middle. When a lens is removed in its capsule in a prepared specimen, as Goldsmith has beautifully demonstrated, the zonule is seen to peel or separate with an elastic "zing," or retraction, first as a small hole, then as a dehiscence, and finally, as a complete peeling away. This can be observed when one is doing the operation itself, as described by Kirby [18] and as seen by many others. Goldsmith's motion pictures, some "stills" of which illustrate his splendid paper,[2] show this "peeling" of the zonule most convincingly and effectively.

BIOMICROSCOPY OF THE ZONULE IN THE LIVING EYE

All of us have seen the zonule fibers in the living eye when there has been a coloboma of the iris or shrinkage or subluxation of the lens. Beautiful plates of the biomicroscopic appearance of the zonule are found in Vogt's "Atlas," [19] in Berliner's "Biomicroscopy of the Living Eye," and in other atlases on the eye.

Trantas,[20] in 1949, described his technique of biomicroscopy of the zonule in the living eye. He used a contact lens and by digital pressure found that it was possible to study a large area of the hyaloid membrane, the posterior zonule, Petit's canal, the zonule of the equator, the ciliary processes, and the anterior zonule. Berliner, in a recent talk in Philadelphia, described his technique and findings, which are very similar to Trantas'. He stated [21]:

> I feel that just as was the case with gonioscopy, we are now on the threshold of an era in which this portion of the living eye, previously out of reach, will become accessible for exami-

18. Kirby, D. B.: Procedures in Intracapsular Cataract Extraction, Am. J. Ophth. **25**:269, 1942; Rupture of the Zonule in Intracapsular Cataract Extraction, Brit. J. Ophth. **33**:3, 1949.

19. Vogt, A.: Textbook and Atlas of Slitlamp Microscopy of the Living Eye, Berlin, Julius Springer, 1931, Vol. 2, p. 738.

20. Trantas, L.: Biomicroscopy of the Zonule in Normal Eyes, Arch. opht. **9**:31, 1949.

21. Berliner, M. L.: Biomicroscopy of the Zonule, Am. J. Ophth. **34**:1756, 1951.

nation. I have only just begun to employ it and hope to report further at a later date. Frequently one is astonished to find how far forward (axial to the equator) the fibers are inserted. . . . I have been able to see deposits on the fibers and in the perilental space. These were blood cells after trauma and exudative cells after inflammation. In one case of exfoliation of the lens capsule flakes could be seen on the zonular fibers.

With the improvement of instrumentation and techniques still in evolution, it is possible that in the future we shall have a method that will permit us to form an idea of the condition of the zonule and the zonular lamella in our cataract patients that will be helpful in the surgical care of these patients.

PRACTICAL APPLICATION

In the age group in which most cataracts are found and operated upon, the eye shows a number of changes due to senescence. The changes that concern us for the moment are those found in (*a*) the lens capsule and zonular lamella, (*b*) the zonule, (*c*) the ora serrata, and (*d*) the vitreous.

It is well known from clinical studies that the lens capsule varies in its thickness, tenacity, and ease of "rupture," i. e., the variability in the readiness with which the zonular lamella separates from its insertion in the capsule as opposed to the readiness of the capsule to tear or rupture. Some of these changes can be seen, or at least suspected, by biomicroscopy. But much further needs to be known on this point, and knowledge regarding nutrition, health, and disease must be painstakingly gathered. The oldest patient on whom I have operated for cataract was 101, and his zonular lamella was most difficult to separate. On the other hand, many of us have operated upon patients of 35 or 40 in whom the lamella separated quite easily, for example, in patients with dinitrophenol cataract. The question, "What conditions affect the cement substance binding the zonule to the capsule of the lens?" needs elucidation. We know little or nothing about how the zonule itself is affected by disease. The new methods of biomicroscopy described by Trantas and Berliner may yield much valuable information.

We have known ever since 1827, when Heusinger first described cystoid degeneration of the retina, which Fischer,[22] in a recent remarkable paper, said was due to capillary perisclerosis, that the retina in the region of the ora serrata becomes fragile with age. We also know that the zonular fibers are attached in this area. Excessive pull on the zonule during cataract extraction or through spasm of the ciliary muscle, e. g., after the instillation of diisopropyl fluorophosphate in some cases, can tear the retina and lead to its disinsertion.

If it is true that the zonule has an intimate connection with the vitreous, and there is strong suspicion that it has, then a pull upon it will lead to its detachment from the retina at the ora serrata and create a favorable situation for later retinal separation.

The posterior lens capsule and zonular lamella and their relation to the anterior hyaloid membrane may now be considered. The smooth, moist convex surface of the lens is in intimate contact with the smooth, moist concave surface of the anterior hyaloid membrane, in Berger's retrolental space, the latter, however, being only potential. There is therefore capillary attraction, which is strong. In addition, if

22. Fischer, F. P.: Retinal Cysts and Cystoid Degeneration of the Retina, Docum. ophth. **5-6**:12, 1951.

the ligamentum hyaloideocapsulare of Wieger is an actual structure, and there is evidence that it is, then there is an actual adhesion between the posterior capsule of the lens and the hyaloid membrane. In addition, there is evidence that embryonic adhesions may also be present. Thus, a rough pull upon the lens can tear the anterior hyaloid membrane and produce characteristic holes, seen many times with the biomicroscope after operation, and lead to herniation of vitreous mass into the anterior chamber. Verhoeff [23] showed, by histologic examination of three eyes, freshly operated upon with his "sliding" technique, that the hyaloid membrane maintained its integrity and was intact. I believe, however, that his choice of specimens was fortuitous and that biomicroscopic examination of eyes after operation by his method would show the same percentage of cases of holes in the anterior hyaloid membrane as do eyes in which the lens was delivered as a tumbler.

Intracapsular cataract extraction can be performed only in three ways: (1) by expression, (2) by pull, and (3) by a combination of push and pull. The first two methods are rarely employed, for experience has shown that they are too brutal. The third is the method practiced almost universally. There has been much discussion of the relative merits of the push and the pull. This point may now be examined in view of our knowledge of the anatomy of the affected parts.

The force of the pull is transmitted to the retrolental space, and through the zonule to the ora serrata and anterior part of the retina, where cystoid degeneration occurs nearly always in the elderly. Such a pull may (*a*) tear the hyaloid membrane, (*b*) tear the retina, producing either a hole or retinoschisis, and/or (*c*) tear the vitreous.

The force of the pressure (e. g., in the pure Smith operation) may (*a*) tear the hyaloid or (*b*) push the vitreous forward, with loss.

Smith,[24] in his bimanual method of pressure, placed a spoon on the corneal wound and pressed backward, thus tilting the upper edge of the lens toward the optic nerve. At the same time, with the muscle hook he pressed below the limbus, tilting the lower edge of the lens forward, and, by the forward drive of the vitreous, peeled off the zonular lamella from the capsule, probably at the posterior portion of the equator first and then the anterior portion. The lens was delivered as a tumbler.

If the erysiphake or the capsule forceps is applied below the anterior pole of the lens, but not too far below to catch the zonular lamella, and the lens is lifted and elevated toward the cornea, so that the lower edge is upward and the upper edge backward, the zonular membrane will be tautly stretched. This method has already been described by Smith,[24] as shown by his Figure 67 *A*. At the same time, by gentle rotation, the adhesions and capillary attraction in Berger's space are relieved.

Pressure, either the point pressure, described by Kirby, or the rotary pressure, described by Smith, or, preferably, a combination of the two in the proper place, which is in and through the cornea just at the limbal ring, will then produce a

23. Verhoeff, F. H.: Conditions of the Ocular Structures Immediately After Removal of the Lens in Capsule as Determined by Microscopic Examination, Tr. Am. Ophth. Soc. **29**:184, 1931.

24. Smith, H.: The Treatment of Cataract, Calcutta, Butterworth & Company, Ltd., 1928, pp. 120 and 162.

beginning separation of the zonular lamella. The pressure must be directed backward, and at the same time toward the feet, in a stripping or milking motion.

The forceps or erysiphake is used to hold the lens in a tilted position. When the lower edge is seen to come forward as the zonule is stripped off, two things are to be done: The most important is to seize the advantage and begin to tuck the cornea under the tumbling lens, and then to guide the delivery of the lens by an exceedingly gentle pull. Tucking of the cornea continues until the lens is delivered. Its action is, first, to assist in peeling off the zonular membrane, and, second, to prevent the vitreous from coming forward below the lower edge of the advancing lens. The final motion is sweeping of the lens away from the cornea at the wound and peeling off of the last remnants of the zonular lamella. In this method, push is estimated at 95% and pull at 5%, but the most effective and important maneuver is the "tucking," described by Smith.

Since vitreous pressure is not utilized by this method to dislocate the lens, a soft eye is no drawback; on the contrary, it is an asset. As a consequence of adequate anesthesia, retrobulbar injection of procaine and hyaluronidase, the O'Brien akinesia combined with hyaluronidase, the use of a superior rectus suture, and employment of the technique based on the fundamental anatomy of the parts described above, the incidence of loss of vitreous is reduced dramatically.

Pearlman, in a recent symposium on cataract surgery held by the Chicago Ophthalmological Society, gave a statistical paper of great interest based on material gathered at the Illinois Eye and Ear Infirmary. He showed that the O'Brien akinesia with procaine and hyaluronidase reduced the loss of vitreous from 12.0%, when hyaluronidase was not used, to 4.3%, when it was.

I might mention here the idea of zonulotomy, which has been played with off and on for years by various authors. The most recent writer, so far as I know, is de Andrade,[25] who coined the word "phakectomy" to describe his technique of "rupturing" the zonule at the 6-o'clock meridian by means of a special zonulotome and then tumbling the lens by pressure. Kirby, whose method of separating the zonular lamella above under direct vision by touching it with the heel of his lens expressor is well known, points out that attempts to do the same thing below, under the iris, and not under the direct vision of the operator, is dangerous.

From a theoretical point of view, and in the hands of surgeons familiar with the instrument, the erysiphake, as pointed out by Harrington, is more efficient in its action of traction on the capsule than is the forceps. There is real danger, however, that if the suction is too strong the posterior capsule ruptures and the surgeon is faced with a most difficult problem.

SUMMARY

The zonular membrane, composed of prismatic fibers, some of which are as long as 7 mm., embedded in a cement substance of unknown composition, is described. There are still controversial points, but enough is known of the anatomy of the zonule to show that it arises in the ora serrata, orbiculus ciliaris, and ciliary processes. Presumably, it has attachments to the anterior edge of the retina, the vitreous, and the hyaloid membrane.

25. de Andrade, L.: Importance of Direct Zonulotomy in the Execution of Total Phakectomy, Ophthalmologica **115**:78, 1948.

The zonular membrane inserts near the equator in three sheets: (*a*) anterior, (*b*) posterior, and (*c*) equatorial, the first two of which form rings of insertions anteriorly about 2 mm. from the equator and posteriorly about 1 mm. from the equator, in the relation of 3:2.

There is a connection between the posterior surface of the lens and the anterior surface of the hyaloid membrane in the hyaloid (retrolental) fossa (space of Berger), which is simply capillary attraction, or actual adhesions formed by means of the ligament of Wieger (ligamentum hyaloideocapsulare), or embryonic fibers, or all three.

Cystoid degeneration of the retina at the ora serrata is almost universal in the age group in which cataract is most frequently found.

Undue traction on the lens capsule during the operation for intracapsular removal of a cataractous lens may, and probably many times does, lead to (*a*) tears in the anterior hyaloid membrane of the vitreous, (*b*) holes or retinoschisis of the retina in the ora-serrata zone, where cystoid degeneration is common, or (*c*) separation of the vitreous from the retina at this point, or all three.

Expression, therefore, rather than pull, is theoretically and practically desirable. Pure expression (Smith) is fraught with danger and is seldom performed.

If the lens is tilted so that its lower edge is forward toward the cornea and slightly rotated side to side, three things occur: (*a*) The capillary attraction of Berger's space (hyaloid fossa) is abolished; (*b*) adhesions between the hyaloid membrane and the posterior lens capsule, if present, are gently separated, and (*c*) the zonular membrane is put on a stretch, particularly at its insertion into the lens capsule.

Point, or rotatory, pressure, or both, directed through the cornea just in front of the limbal ring will start the peeling of the zonular lamella from the capsule. The pressure is exerted backward and down in a milking or peeling fashion.

The eye can, and should, be "soft" when this method is used. If the O'Brien facial-nerve block with procaine and hyaluronidase is used, the incidence of loss of vitreous is lowered.

The tucking of the cornea under the tumbling lens as it is delivered, described years ago by Col. Henry (Jullunder) Smith, is of the utmost importance in the safe delivery of a tumbling lens.

Biomicroscopy of the living eye with new instruments and techniques may yield much important information regarding the state of the zonular membrane.

OCULAR COMPLICATIONS IN THE RAT MADE DIABETIC WITH ALLOXAN

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CATARACTS in rats made diabetic by pancreatectomy were observed by Foglia and Cramer [1] in 1944, and in the same year Bailey, Bailey, and Leech [2] reported cataracts in rats made diabetic with alloxan. Since these earlier studies, many investigators have obtained cataracts in diabetic rats. Most workers have pointed out that high blood sugar levels are imperative for cataract formation. This has been stressed in the recent publications of Sterling and Day [3] and Patterson.[4] By altering experimental diets, mainly by reducing the carbohydrate content, Charalampous and Hegsted [5] and Rodriguez and Krehl [6] have prevented cataract formation or delayed its onset in the diabetic rat. Kok-van Alphen [7] found that if the diabetes in the rat was controlled with insulin, cataract failed to develop. The work cited demonstrates that cataract occurs either because of failure of the lens to metabolize glucose or because the high aqueous sugar which results from this faulty metabolism is a significant cataractogenic factor itself.

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These studies were aided by grants from the National Council to Combat Blindness upon recommendation of its Medical Consultants and the Central Scientific Funds, State University of Iowa.

1. Foglia, V. G., and Cramer, F. K.: Experimental Production of Diabetic Cataract in the Rat, Proc. Soc. Exper. Biol. & Med. **55**:218, 1944.

2. Bailey, C. C.; Bailey, O. T., and Leech, R. S.: Alloxan Diabetes with Diabetic Complications, New England J. Med. **230**:533, 1944.

3. Sterling, R. E., and Day, P. L.: Blood Sugar Levels and Cataract in Alloxan-Treated Galactose-Fed and Xylose-Fed Weanling Rats, Proc. Soc. Exper. Biol. & Med. **78**:431, 1951.

4. Patterson, J. W.: The Course of Diabetes and Development of Cataracts After Injection of Dehydroascorbic Acid and Related Substances, Am. J. Physiol. **165**:61, 1951.

5. Charalampous, F. C., and Hegsted, D. M.: Effect of Age and Diet on the Development of Cataracts in the Diabetic Rat, Am. J. Physiol. **161**:540, 1950.

6. Rodriguez, R. R., and Krehl, W. A.: Influence of Diet and Insulin on the Incidence of Cataracts in Diabetic Rats, Yale J. Biol. & Med. **24**:103, 1951.

7. Kok-van Alphen, C. C., and Cohen, E. M.: The Occurrence of Cataract in Alloxan Diabetic Rats, Acta physiol. et pharmacol. neerl. **1**:400, 1950.

In earlier experiments in which nicotinic acid was used to influence the fat metabolism of rats made diabetic with alloxan,[8] certain differences in the ocular complications in these animals were observed. The present study was undertaken in order that we might investigate more closely the effects of nicotinic acid[9] on the development and progression of cataract and other ocular complications in the rat with alloxan diabetes.

METHODS

Adult male rats of the Long-Evans strain were fasted for 48 hours and given injections of 100 to 115 mg. of alloxan per kilogram of body weight. Twenty-one rats which were severely diabetic two weeks after injection were fed a synthetic diet having the following composition:

Casein	350 gm.
Sucrose	600 gm.
Corn starch	600 gm.
Yeast (Pabst)	200 gm.
Salt mixture[9a]	50 gm.
Hydrogenated cottonseed oil (Crisco)	100 gm.
Cottonseed oil	100 gm.
Choline	400 mg.
Haliver oil	4 cc.

In one phase of the experiment, some of the animals were fed this diet plus 1% nicotinic acid.

Blood sugar levels were determined by the method of Somogyi.[10] Urine volumes and food intake were measured daily for three days each week. Urinary acetone levels were determined at weekly intervals by Van Slyke's gravimetric method. The rats were weighed once a week. The density and progression of cataracts were determined with an ophthalmoscope at weekly intervals. The density of the cataracts was ascertained for each eye and recorded as 1 to 4. The first evidence of lens opacity was 1, and the maximum opacity, 4. The average density of cataracts was obtained by dividing the sum of the densities by the number of eyes examined.

Recently Bellows and Shoch,[11] using a slit lamp were able to discern the first signs of cataract formation in the diabetic rat about 14 days after the injection of alloxan; but since the present study was not particularly concerned with the minute morphology of the developing cataract, ophthalmoscopic examination was used.

The animals were originally paired, as nearly as possible, so that they had similar blood sugar levels, urine volumes, and body weights. One of each pair was fed the basal diet and the other the nicotinic-acid diet.

RESULTS

The mortality rate in the animals was high because of the uncontrolled diabetes. Six of the 21 rats had died by the 22d week, and only 3 survived the 46 weeks of the study. The severity of the diabetes was evident not only from the nonfasting blood sugar levels, but also from the food intake and urine volumes, which are shown in Figure 1. There was considerable variation in average urine volumes, but the food intake was fairly constant, after the fourth week, for the entire period of the study.

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8. Janes, R. G.: Comparative Study of the Ketogenic Activity of Certain Niacin Compounds, Proc. Soc. Exper. Biol. & Med. **75**:246, 1950. Janes, R. G., and Boeke, L.: Action of Priscoline and Niacin on Certain Phases of Fat and Carbohydrate Metabolism, Am. J. Physiol. **167**:799, 1951.

9. The nicotinic acid was supplied through the courtesy of Hoffmann-LaRoche, Inc., Nutley, N. J.

9a. Hubbell, R. B.; Mendel, L. B., and Wakeman, A. J.: A New Salt Mixture for Use in Experimental Diets, J. Nutrition **14**:273, 1937.

10. Somogyi, M.: Determination of Blood Sugar, J. Biol. Chem. **160**:69, 1945.

11. Bellows, J. G., and Shoch, D. E.: Alloxan Diabetes and the Lens, Am. J. Ophth. **33**:1555, 1950.

Two mildly diabetic rats were not included in the study because their blood sugars ranged from 140 to 160 mg. per 100 cc. and after 20 weeks the animals failed to show any abnormalities in the lens.

The first manifestation of cataract was usually seen in the posterior cortical or posterior subcapsular region and was characterized by small punctate opacities grouped in a linear arrangement (Fig. 2*a*). In general, opacities in the lens appeared simultaneously in both eyes of a particular animal, but in some instances one eye showed some delay in cataract formation. At the fourth week following alloxan injection, 13 eyes of the 42 studied showed 1 + cataracts. Subsequently, there was an enlargement of this central opacity, and in certain cases peripheral opacities could be observed. At this stage it was still possible to see the vascular pattern in the fundus (Fig. 2*b*). In the third stage the opacification had advanced to a point at which the fundus could be seen only with difficulty, mainly because of diffuse cortical changes (Fig. 2*c*). The fourth, and final, stage was characterized by opacification of the lens; in most instances the lens was swollen and contained several water slits (Fig. 2*d*).

Weeks	4th	6th	8th	10th	12th	14th	16th	18th	20th	22nd	24th	26th	28th	30th	32nd	34th	36th	38th	40th	42nd	44th	46th
Average density of cataracts	.31	.39	1.2	1.2	1.8	2.1	2.4	2.6	3.1	3.3	3.4	3.6	3.4	3.4	3.4	3.5	3.5	3.6	3.6	3.5	3.5	3.5
Urine volume (cc/24 hrs.)	211	229	180	188	197	191	198	214	221	206	216	210	206	190	176	184	174	173	203	207	200	175
Food intake (gm./24 hrs.)	43	38	30	31	31	29	32	33	35	32	32	30	30	29	28	30	30	28	30	34	36	32
Number of surviving animals	21	21	20	17	17	17	16	15	16	15	14	12	12	7	7	6	6	6	6	5	3	3

Average Blood Sugar 499 mg. /100 Cc. max. 790 / min. 305 – 22nd. week Average Blood Sugar 501 mg. /100 Cc. max. 724 / min. 292 – 36th. week

Fig. 1.—Development of cataract in nicotinic-acid-fed and stock-fed rats made diabetic with alloxan. The average density did not reach 4 because in one animal only a 2+ cataract developed.

Although it is not evident in Figure 1, cataractous changes were present in all rats by the 8th week and, with the exception of one rat, had reached their maximum density at approximately the 24th week. The single exception, a severely diabetic rat with blood sugar levels at or near 400 mg. per 100 cc., had only a 2 + cataract at 46 weeks.

The fundi were examined at weekly intervals in an attempt to observe any retinopathy or changes in the appearance of the vascular pattern. Only one rat, which was receiving the basal diet, had a striate hemorrhage in the fundus, and this appeared in the eighth week. By the 14 to the 16th week the fundi could not be seen clearly because of the cataracts. In an attempt to alleviate this difficulty, we performed cataract extraction, either extracapsular or intracapsular, in some of the animals. However, regardless of the method used, surgical intervention was followed by vascularization and opacification of the cornea and atrophy of the globe.

A comparison was made of rats fed the basal diet and those fed the nicotinic-acid diet (Fig. 3). The animals on the nicotinic-acid diet showed a slower progression of cataracts. Maximum opacities were seen at the 24th week. The lower average lens opacity in the nicotinic-acid-fed group was due to the fact that one rat receiving the nicotinic-acid diet had only a 2 + cataract. By the fourth week of the study, the rats

given the basal diet showed the severer diabetic signs, and these continued throughout the study. The blood sugar levels, for instance, on the 20th week showed average values of 656 mg. per 100 cc. for rats receiving the basal diet and of 433 mg. per 100 cc. for those receiving the nicotinic-acid diet. The urine volumes and food intake were higher throughout the study for the animals eating the basal diet.

The data were examined for a typical pair of rats with similar blood sugar levels, urine volumes, and food intake, one being fed the basal diet and the other the high

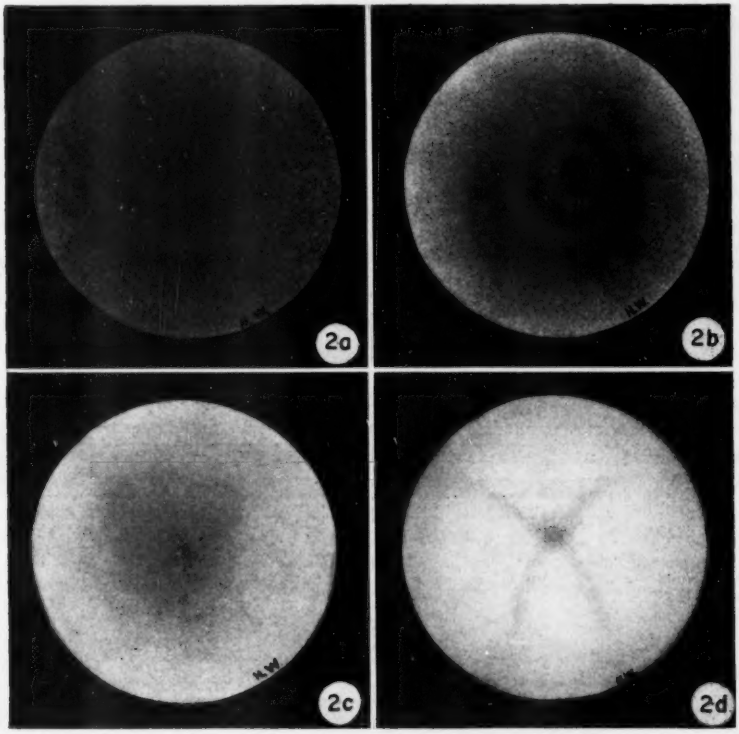

Fig. 2.—The appearance of cataract with the ophthalmoscope in rats made diabetic with alloxan: *a* (Stage 1), posterior subcapsular opacities; *b* (Stage 2), increased subcapsular opacities and diffuse cortical haze, more marked peripherally; *c* (Stage 3), increased opacity due to generalized cortical haze; *d* (Stage 4), complete opacity with water slits.

nicotinic-acid diet (Fig. 4). Again, the rate of cataract formation was somewhat slower in the nicotinic-acid-fed animals. Furthermore, there were a reduced food intake and lower urine volumes in the latter animals. The blood sugar values at the 6th, 15th, and 25th weeks were 400, 596, and 710 mg. per 100 cc., respectively, for the rat receiving the basal diet and 440, 490, and 385 mg. per 100 cc., respectively for the rat fed the high nicotinic-acid diet. There appeared to be no correlation between urinary acetone levels and cataract formation.

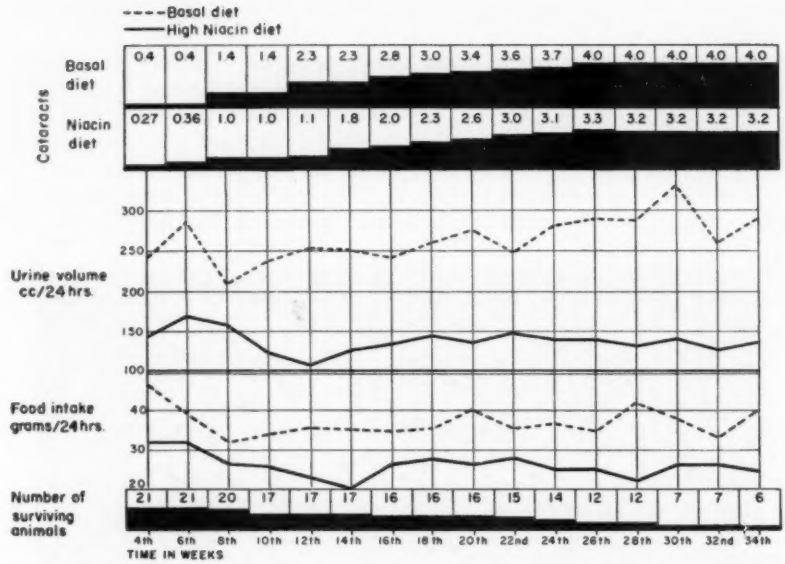
----Basal diet
——High Niacin diet
Cataracts
Basal diet
Niacin diet
0.4 0.4 1.4 1.4 2.3 2.3 2.8 3.0 3.4 3.6 3.7 4.0 4.0 4.0 4.0 4.0
0.27 0.36 1.0 1.0 1.1 1.8 2.0 2.3 2.6 3.0 3.1 3.3 3.2 3.2 3.2 3.2
Urine volume cc/24 hrs.
300
250
200
150
100
Food intake grams/24 hrs.
40
30
20
Number of surviving animals
21 21 20 17 17 17 16 16 16 15 14 12 12 7 7 6
4th 6th 8th 10th 12th 14th 16th 18th 20th 22nd 24th 26th 28th 30th 32nd 34th
TIME IN WEEKS

Fig. 3.—Progression in formation of cataract in diabetic rats receiving basal and high nicotinic-acid diets.

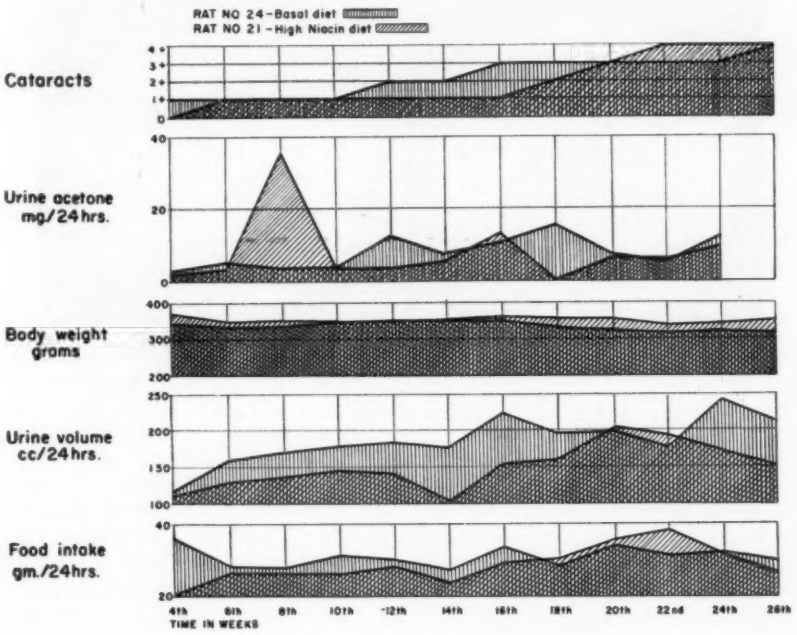

Fig. 4.—Formation of cataract in individual diabetic rats.

Massive intraocular hemorrhages were observed in seven animals, two of which had received the high nicotinic-acid diet. The hemorrhages, besides being more frequent, occurred earlier in the rats receiving the basal diet.

COMMENT

The injection of alloxan intraperitoneally readily produced severe diabetes in our experimental animals, and after six weeks the average blood sugar in the group of 21 rats was over 500 mg. per 100 cc.

The present studies confirm the observations of others [12] that rats must have rather severe diabetes for some time before cataract will develop. In the two animals with blood sugars ranging from 140 to 160 mg. per 100 cc., no cataracts were noted after 20 weeks. It required four to eight weeks after alloxan injections for the remaining animals to exhibit cataractous changes that could be observed with the ophthalmoscope.

It appears that the nicotinic-acid-containing diet caused some amelioration of the diabetic manifestations in the animals, and, as would be expected, the occurrence and progression of cataract in the nicotinic-acid-fed animals were delayed. This may have been due to alteration of the diabetic state resulting from the lowered food (carbohydrate) [13] intake, or to a more specific action of the nicotinic acid. Such an effect could occur through its vasodilator action or through its being incorporated in cozymase (coenzyme I), which is important in metabolism of carbohydrates and fats. The evidence so far accumulated in this study does not permit any conclusion concerning the effect of nicotinic acid.

Changes typical of diabetic retinopathy in man were not noted in these animals. As mentioned earlier, only one animal showed a striate hemorrhage in the retina during the eighth week. With diabetes of this severity, one would expect a considerable vascular disturbance in the retina, but in none of the eyes were changes in the arteries or veins observed. Perhaps if the retinas could have been followed for a longer period, these changes would have been evident.

Intraocular hemorrhage usually began as a small hyphema; bleeding continued and filled the anterior chamber within two days. The hemorrhage in some instances became so massive that the globe was distended, and in a few instances the eyeball ruptured. The blood absorbed slowly and resulted in corneal vascularization and opacification. A study of the histology of these eyes is being investigated and will be the subject of a future paper.

SUMMARY

1. In 21 rats made severely diabetic with alloxan, early cataractous changes were noted at one month and complete opacity of the lens at six months.

2. When diets containing excess nicotinic acid were fed, there was some delay in cataract formation. This may have resulted from the lower food intake of the nicotinic acid-fed group or from some effect from the nicotinic acid itself.

3. Retinal change, consisting of a single hemorrhage, was observed in only one instance. After cataractous changes occurred, detailed observations of the fundus was impossible.

4. Massive intraocular hemorrhage occurred in five of the animals fed the basal diet and in two animals fed the nicotinic-acid diet.

12. Sterling and Day.[3] Patterson.[4]

13. Charalampous and Hegsted.[5] Rodriguez and Krehl.[6]

SYNDROME OF CARTILAGE PATHOLOGY, DESTRUCTIVE IRIDOCYCLITIS, MULTIPLE JOINT DISLOCATIONS

Comparison with Concurrent Eye and Joint Diseases Described in Literature

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CHRONIC destructive iridocyclitis with or without cataract formation occasionally is seen associated with severe ankylosing rheumatoid arthritis. A number of other diseases of joints are associated with iridocyclitis, as described later. The patient who is the subject of this report, however, presented concurrent destructive iridocyclitis, atrophy or deformity of body cartilages, and multiple joint dislocations, without destruction of either bone or joint surface. This syndrome was not familiar to me, and I have been unable to find anything just like it described in the literature.

REPORT OF A CASE

Mrs. H. E., aged 61, when seen first, in May, 1949, complained of rheumatism and blindness. She had been considered well until January, 1947, when there developed a sequence of symptoms which was initiated by a feeling of warmth on the medial aspect of the knees. This was followed by difficulty in her assuming the erect position after kneeling; soon pain and swelling were noted in the knees. This process of pain, swelling, and limitation of motion progressed to involve the shoulders, wrists, ankles, and many of the small joints of the fingers and toes, as well as the knees.

She was hospitalized in March, 1947, and again in October, 1947, when she was given fever therapy and certain antibiotics. The diagnosis on discharge was chronic rheumatoid arthritis, chronic cervicitis, and secondary anemia. She complained a little of her eyes during this stay, and I saw her briefly one day. The only objective finding, on examining her in bed, was congestion of the bulbar conjunctiva. In the light of what followed, this was probably due to scleritis.

During the interim between her hospitalization in 1947 and my examination in May, 1949, several things occurred. The pain and swelling of the joints practically disappeared, and she was able to walk with crutches. Many of the joints of the hands and feet remained deformed, but the larger joints seemed about normal. At one time both external ears were said to have swollen like balloons and to have drained fluid. The patient's voice changed from one of high-pitched quality to one having a masculine character. Her vision began to fail in the early part of 1948, a few months after she left the hospital, and this loss progressed steadily to blindness.

The patient's past history taken at this time revealed only that she had had mastitis and pneumonia 30 years previously. With the latter alopecia developed. She had had no other illnesses and no previous rheumatism. However, she claimed to have had an unusual degree of suppleness of her joints, which she declared exceeded that of her young daughters. When questioned, she said she did not feel that this suppleness was abnormal in degree.

It was learned that her husband and seven of her eight children were living and well.

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Examination at the first visit (May 27, 1949) showed a cheery, comfortable patient, who sat in a chair like an invalid. She spoke in an unusually deep voice for a woman. The tactile tension of the eyes was low, being lower in the right eye than in the left; and both eyes were pale, save for one or two rather prominent veins crossing the sclera at the outer canthus. The extraocular movements seemed normal. The corneas were clear; the anterior chambers were shallow (the right more than the left); the irises bulged forward, as in iris bombé, and were atrophic, Grade 2 to 3. The pupillary margins were adherent to the lens capsule, and both lenses were cataractous, Grade 3. Vision was limited to light perception, being somewhat better in the left eye than in the right. The pupils were stationary, probably from adhesions. There were many pigment granules on the lens capsule in the pupillary area.

On examining the ears (Fig. 1) I noted that both pinnas were thickened, deformed, and compressed. The auditory canals were clean; the right drum membrane was pale and intact, but the left membrane was red, Grade 1. Hearing was noticeably impaired. An audiogram taken subsequently, indicated perception deafness.

There was atrophy of the cartilages of the nose—the septal, alar, and upper lateral cartilages (Fig. 1)—with a resultant saddle deformity of the lower part of the bridge and drooping and softening of the tip. On anterior rhinoscopy, the septal cartilage appeared to be entirely absent

Fig. 1.—Profile view, showing the deformity of the nose and ear, resulting from involvement of the alar, septal, and upper lateral cartilages of the nose and the concha of the pinna. The nasal cartilages seemed to have disappeared entirely, whereas the cartilages of the ear were left greatly thickened and deformed.

and the septum very soft and mobile. The nasal mucous membranes appeared normal; the breathing spaces were ample. Examination of the throat revealed nothing remarkable. The mandible moved freely, but there seemed to be some discomfort in the mandibular joint when the jaw was opened widely. On palpation the larynx seemed to be somewhat flattened in an anteroposterior direction.

Examination of the thorax showed the lower two-thirds of the sternum to be abnormally mobile at the manubrial joint. The rib cartilages all seemed to be soft, and the sternum retracted on inspiration. The patient could dislocate the left sternoclavicular joint at will on manipulation of the shoulder. The lower end of the ulna (Fig. 2 *A*, *B*, and *C*) in each arm was prominent and obviously dislocated. The phalanges were dislocated ventrally from the corresponding metacarpal bones, resulting in shortening of many fingers. Similar deformities were present in the toes. Superficial inspection did not reveal any deformity of the shoulders, elbows, knees, or pelvic joints. Atrophy of the skin was rather pronounced for a person of her age. The alopecia, which had appeared 30 years earlier, was evident.

It was thought that the patient had (1) quiescent plastic iridocyclitis and bilateral degenerative cataract, with other degenerations probable within the eyes; (2) quiescent polyarthritis

with abnormal mobility of the joints and multiple dislocations, and (3) an affection of the cartilages, resulting in atrophy and degeneration.

Because there was light perception in both eyes, cataract extraction, though fraught with hazards, was thought worthy of consideration.

The patient was studied further on July 21, when she was brought to the office and examination made with a corneal microscope. On the right, this study revealed punctate opacities in the superficial layers of the cornea over the medial pupillary area, but the remainder of the cornea was clear. The iris was atrophic, Grade 3. There seemed to be adhesions over much of the posterior surface of the lens. Pigment was present on the anterior lens capsule, and numerous blood vessels were seen in the iris, many of them crossing the edge of the pupillary margin from behind to the anterior surface. The lens was cataractous, Grade 4, and the anterior chamber was almost empty. On the left, the cornea showed a number of old keratic precipitates on the posterior surface and fine, lace-like opacities on the anterior surface, but otherwise it was reasonably clear. The anterior chamber was about one-half the normal depth. There was a moderate degree of iris bombé; the iris was similar to that of the right eye except that the atrophy and vascularity were not so pronounced in the left eye. There was no pupillary reaction, and the lens was cataractous, Grade 4. Intraocular tension, measured with both the Schiøtz and the McLean tonometer, was 0 in the right eye and 13 mm. in the left.

Subsequently, the patient was photographed (Figs. 1 and 2); roentgenograms (Fig. 3) of many of the joints were taken, and blood studies were instituted. On August 24, the sedimentation rate was 13 mm. in one hour; the red blood cells numbered 3,980,000, with 85% hemoglobin; there were 7,650 leucocytes and a normal differential count except for 11% eosinophiles (49% polymorphonuclear neutrophiles, 35 lymphocytes, 1 basophile, 4 monocytes, and 11 eosinophiles). The urine was normal; there was no alkaptonuria. The blood phosphorus was 4.06 mg., and the blood calcium 10.75 mg., per 100 cc.

On Feb. 15, 1950, a preliminary iridectomy was done on the left eye. It was deemed wise to see how the eye would tolerate surgery before an attempt was made to free and extract the lens. The pathologist reported that there was no significant inflammatory or neoplastic change in the small piece of iris received for examination. It did, however, exhibit atrophic changes and thickening and hyalinization of the walls of the small vessels. The postoperative course was uneventful. When she was seen on March 7, the anterior chamber of the left eye was very shallow; there was some congestion of the iris, but not appreciably more than before the operation. The tactile tension in the left eye was low, but still somewhat higher than that of the fellow eye; when measured on the McLean tonometer it was 0 in the right eye and 6 mm. in the left eye.

About April 1, 1950, there occurred the first noteworthy exacerbation since the remission of symptoms after her illness, three years earlier; this exacerbation consisted in moderate swelling and pain in the joints; the eyes remained quiet. Laboratory data were procured when the patient was hospitalized for several days in May, 1950. Urinalysis was noncontributory, showing only 0 to 8 white cells and 0 to 1 red cell, per cubic millimeter. The icterus index was 7 units; erythrocytes numbered 4,100,000; the hemoglobin was 12 gm. per 100 cc., or 84%. There were 6,900 leucocytes; a differential white cell count showed 2 basophiles, 3 eosinophiles, 1 stab cell, 54 segmented polymorphonuclear neutrophiles, 37 lymphocytes, and 3 monocytes. The sedimentation rate was 53 mm. an hour. The cephalin-cholesterol flocculation test gave a 3+ reaction in 24 hours and a 4+ reaction in 48 hours. Plasma albumin was 4.28 gm. per 100 cc., and plasma globulin, 2.40 gm. per 100 cc. Bence Jones protein was not found in the urine. A second determination of the sedimentation rate, one week after the first, showed 44.5 mm. an hour. Tests for brucellosis were reported as negative, and a blood Wassermann test, done elsewhere, gave a negative reaction.

A biopsy specimen taken from the cartilage of one of the external ears was studied for amyloid by three pathologists, none of whom was very certain as to what it showed.

Roentgenograms (Fig. 3) were made of the pelvis, the lumbar portion of the spine, the left shoulder, the right knee, the right hand, and the right wrist. All the bony structures showed marked osteoporosis, without selection of any portion of the bones. There were conspicuous thinning of the bony cortex in all bones and slight narrowing of the hip-joint spaces, but the bony contours were normal. The sacroiliac joints were normal, and the pelvis was normal

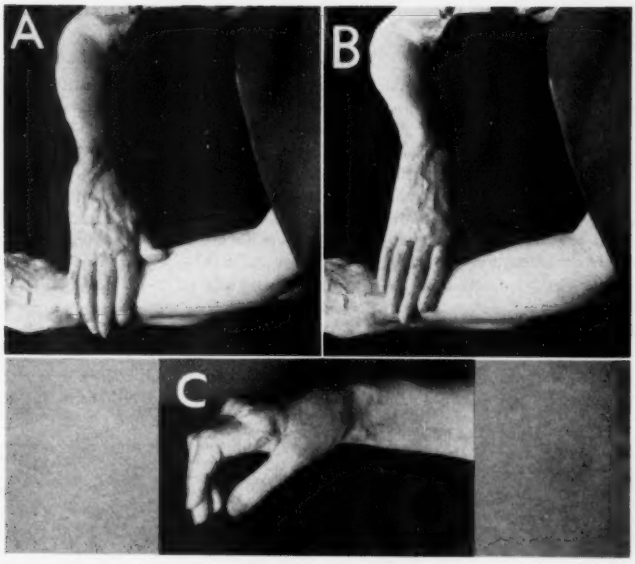

Fig. 2.—Deformity of the hand and wrist resulting from multiple dislocations due to extreme laxness of the joint ligaments. *A*, ulna at rest; *B*, ulna lifted; *C*, dislocation of proximal phalanges toward the palmar surface of the hand. Neither the carpals nor the phalanges showed any enlargement or ankylosis, either clinically or roentgenologically.

Fig. 3.—Roentgenographic views of one hand, showing the dislocations. There is extensive osteoporosis; otherwise the bony contours all appear normal except for the lower end of the ulna. The interphalangeal spaces appear somewhat narrowed, as though the cartilages were thinned or gone.

except for osteoporosis, as were the left shoulder joint and the right knee. There was considerable fluid within the knee joint and the suprapatellar bursa, which was greatly distended. No significant narrowing of the joint spaces (wrist, knee, and hip) was noted, with the possible exception of the phalanges; but there was complete anterior dislocation of the metacarpophalangeal joints, save for those of the thumb. The ulna was dislocated posteriorly, with atrophy and possibly some destruction at the distal end. One small fragment was loose in the soft tissues. The roentgenologist concluded that many of the findings were similar to those in rheumatoid arthritis but differed in that there was no marked abnormality of bone other than osteoporosis, no destruction of joints, and no ankylosis. There were severe deformities, but these seemed to be due entirely to dislocation, and not to bony enlargement or other abnormality (Fig. 4).

The exacerbation gradually subsided, and the patient returned to her previous state in July, 1950. The left cataractous lens was extracted Nov. 29, 1950. The adhesions between the iris and the lens separated rather readily, and the lens, which was found to be almost spherical, was extracted intracapsularly without great difficulty. Upon removal of the lens, a white, dense retrolental membrane was seen stretching across the anterior portion of the vitreous chamber. The corneal flap was lifted, and an incision was made through the center of this membrane.

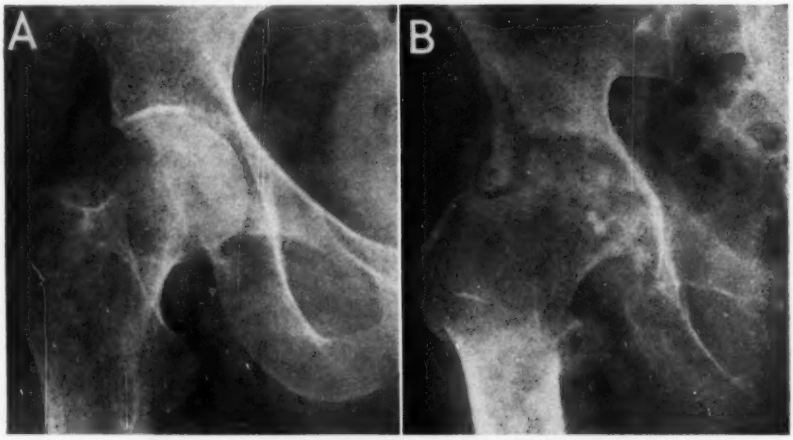

Fig. 4.—Comparison of the hip joints in the case here reported (*A*) and a case of usual rheumatoid arthritis with complicating iridocyclitis (*B*). In the case here reported (*A*) there was no joint destruction, and vision had been lost in both eyes. The joint in *B* shows extensive destruction of the acetabulum and the head of the femur, with lipping of the joint and ankylosis; the patient has lost vision in one eye. The involvement and destruction of the ocular structures were more extensive in the case here reported (*A*) than in the other (*B*). Both patients were bedridden, the one (*A*) because of dislocations and the other (*B*) because of extensive ankylosis. (Fracture, just below the trochanter in *B* was sustained on manipulation incidental to cystoscopy.)

Instead of normal, clear vitreous, a brownish-yellow fluid appeared. No vitreous was seen. The postoperative course was uneventful, the eye healing with very little reaction. When the bandage was removed, the patient complained rather bitterly of strong light; but, for all practical purposes, the eye remained entirely blind. Apparently, the vitreous, retina, and ciliary body had been irreparably damaged by the disease process. The eye remained soft. This would ordinarily lead one to assume that there was a dearth of aqueous formation. However, an air bubble left in the anterior chamber disappeared at about the same rate as it does in the ordinary case of cataract extraction.

Examination of the eyes on June 8, 1951, showed normal lids bilaterally. The conjunctival surfaces were not remarkable. Tactile tension was zero in both eyes. The right cornea was clear, and the sclera was not congested but contained three prominent vessels running roughly parallel

with the medial, lateral, and inferior rectus muscles. These vessels began just a little posterior to the limbus and extended backward over the globe. The anterior chamber was practically collapsed. The iris was atrophic, Grade 3, and the lens was cataractous, Grade 4. On the left, there were vessels similar to those described on the right, together with slight circumcorneal congestion. The cornea was clear in the central portion, but close to the limbus, especially above, it was somewhat cloudy. A few faint radiating folds crossed the cornea from 12 o'clock downward (just such folds as one sees in the cornea when a corneoscleral suture has been pulled too tightly at the end of operation). These radiating folds were indicative of great softness of the eye. The anterior chamber was deep in the central portion; the peripheral portion seemed to be very shallow. The coloboma of the iridectomy was not seen very well because of the cloudiness in the upper part of the cornea. The retrolental membrane was still present and still lay in a plane somewhat posterior to that of the iris. The iris was atrophic, Grade 3. There was no pupillary reaction in either eye, and apparently light perception had been lost in both.

REVIEW OF LITERATURE

Although there is an extensive literature on concurrent eye and joint disease,[1] it is somewhat confusing, and a search failed to reveal any literature on a syndrome involving cartilages outside the joints. Godtfredsen,[2] of Copenhagen, published a

TABLE 1.—*Incidence of Ocular Symptoms Complicating Joint Diseases* *

	Conjunctivitis, %	Iritis, %	Keratoconjunctivitis Sicca Syndrome, %
Acute joint diseases			
Rheumatic fever	5-10	4-5	..
Gonorrheal arthritis	10	5	..
Reiter's disease	80	10	..
Uratic arthritis	..	2	..
Chronic joint diseases			
Primary progressive chronic polyarthritis	..	2-5	10
Still's disease	..	20	..
Ankylopoietic spondylarthritis (Bechterew-Strümpell-Marie disease)	..	15-50	..

* After Godtfredsen.[2]

1. Bentley, N.: Iritis and Iridocyclitis, J. Mich. M. Soc. **49**:166-173 (Feb.) 1950. Berens, C.; Rothbard, S., and Angevine, D. M.: Cultural Studies on Patients with Uveitis and Other Eye Diseases, Am. J. Ophth. **25**:295-301 (March) 1942. Eggers, H.: Necroscleritis Nodosa Associated with Chronic Rheumatoid Polyarthritis: Report of a Case, Arch. Ophth. **23**:501-506 (March) 1940. Harbater, M.: Scleromalacia Perforans: Report of a Case, ibid. **41**:183-187 (Feb.) 1949. Kurnick, N. B.: A Rare Syndrome of Band-Shaped Keratitis and Arthritis, Am. J. Dis. Child. **63**:742-747 (April) 1942. Mann, W. A., and Markson, D. E.: A Case of Recurrent Iritis and Episcleritis on a Rheumatic Basis Treated with ACTH, Am. J. Ophth. **33**:459-461 (March) 1950. Novoa-Recio, F. E.: Importance of X-Rays and Red-Blood-Cell Sedimentation Rate in the Diagnosis and Treatment of Different Forms of Arthritis Complicated with Iritis, Arch. oft. Buenos Aires **16**:36 (Jan.) 1941; abstracted, Am. J. Ophth. **25**:761-762 (June) 1942. Recordon, E. G.: Modern Views on the Causation and Treatment of Iridocyclitis, M. Press (Eng.) Oct. 2, 1946, pp. 245-248. Smoleroff, J. W.: Scleral Disease in Rheumatoid Arthritis: Report of 3 Cases, in One of Which Both Eyes Were Studied Post Mortem, Arch. Ophth. **29**:98-108 (Jan.) 1943. Sorsby, A., and Gormaz, A.: Iritis in the Rheumatic Affections, Brit. M. J. **1**:597-600 (April 20) 1946. Wong, R. T.: Band-Shaped Opacity of the Cornea Associated with Juvenile Atrophic Arthritis: Report of a Case, Arch. Ophth. **26**:21-24 (July) 1941.

2. Gotfredsen, Erik: Pathogenesis of Concurrent Eye and Joint Diseases, Brit. J. Ophth. **33**: (May) 1949.

study of concurrent eye and joint disease in 1949. He classified rheumatic joint disease complicated by ocular symptoms, as indicated in Table 1. He listed further diseases with concurrent symptoms referable to the eyes, joints, skin, and mucous membranes, as seen in Table 2.

Reiter's syndrome consists in polyarthritis, urethritis, and conjunctivitis. It was especially prevalent after World War II. Still's disease (multiple rheumatoid arthritis) is a chronic polyarthritis of children, especially girls, which leaves iris adhesions. Ankylopoietic spondylarthritis (Bechterew-Strümpell-Marie disease) involves the sacroiliac joints and the spine and is frequently complicated by iritis. The ocular symptoms are infrequent in the common joint diseases and frequent in the rarer diseases. The pathogenesis is probably the same for both the eye and the joints and is likely allergotoxic in nature. Phlyctenules, episcleritis, Aschoff nodules in the heart, and rheumatic nodules on the skin are all similar histologically. They show polymorphonuclear neutrophiles, small lymphocytes, and epithelioid cells,

TABLE 2.—*Diseases with Concurrent Symptoms from Eyes, Joints, Skin and Mucous Membranes* *

	Eyes	Joints	Skin	Mucous Membranes (Stomatitis; Balanitis)
Virus diseases of obscure origin				
Reiter's disease	+	+	+	+
Stevens-Johnson syndrome	+	(+)†	+	+
Foot-and-mouth disease	+	?	+	+
Behcet's syndrome	+	(+)	+	+
Acute disseminated lupus erythematosus	+	+	+	+
Measles; chickenpox	+	(+)	+	+
Bacterial diseases				
Gonococcic sepsis	+	+	(+)	+
Streptococcic sepsis	(+)	+	+	+
Intoxications				
"Sanocrysin" (gold sodium thiosulfate); arsenicals	+	(+)	+	+
Serum sickness	+	+	+	+

* After Godtfredsen.[2]
† (+) means "less significant."

which are sometimes polymorphonuclear. Godtfredsen stated that the blood-aqueous and the blood-synovial barrier are similar and that the ciliary processes of the eye and the synovia of the joints are alike susceptible to streptococci.

The Stevens-Johnson syndrome is a form of exudative erythema multiforme with conjunctivitis and stomatitis. Behcet's syndrome involves ulceration of the genitals and mouth, together with uveitis and joint disease.

It has been suggested that this condition may be a case of Ehlers-Danlos syndrome (cutis hyperelastica).[3] It is true that the hyperlaxity and hyperextensibility of the joints might suggest this, but none of the other characteristics is present. Moreover, the Ehlers-Danlos syndrome usually occurs in youth, whereas this

3. Benjamin, B., and Weiner, H.: Syndrome of Cutaneous Fragility and Hyperelasticity and Articular Hyperlaxity, Am. J. Dis. Child. **65**:247-257 (Feb.) 1943. Freeman, J. T.: Ehlers-Danlos Syndrome, ibid. **79**:1049-1056 (June) 1950. Johnson, S. A. M., and Falls, H. F.: Ehlers-Danlos Syndrome: A Clinical and Genetic Study, Arch. Dermat. & Syph. **60**:82-105 (July) 1949. Pray, L. C.: Cutis Elastica (Dermatorrhexis, Ehlers-Danlos Syndrome), Am. J. Dis. Child. **75**:702-711 (May) 1948.

patient's trouble did not have its inception until the end of the sixth decade of life. In addition, this patient has suffered destructive iridocyclitis with blindness and damage or destruction of certain cartilages, none of which are commonly associated with the Ehlers-Danlos syndrome. In my opinion, the latter syndrome can be ruled out.

SUMMARY

A syndrome is described which seems to be unique. It consists of destructive iridocyclitis with cataract formation and other degenerations within the eyes, hyperlaxity and dislocation of many joints, without destruction of joint surfaces, and the involvement of other body cartilages in atrophy or other destructive changes. The changes in the eyes began as slight discomfort and congestion and progressed to severe iridocyclitis with keratic precipitates, atrophy of the iris, mature cataract, and extreme hypotony. There was a retrolental fibrous layer in the one eye, which was operated upon. All vision was eventually lost in both eyes. The articular changes seemed at first to be related to rheumatoid arthritis but differed in that there was no ankylosis of the joints and little or no damage to the joint surfaces. On the other hand, the joint capsules were so exceedingly lax that multiple dislocations had resulted. The cartilages of the nose had disappeared as far as can be determined. The cartilages of the ear became hypertrophic and extremely deformed. The rib cartilages became very soft and the joints about the sternum amazingly mobile. The condition does not seem to fit into any of the syndromes of concurrent eye and joint disease which are described in the literature.

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VISUAL DEFECTS IN THE DEAF CHILD

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AN ANALYSIS of the findings in the ophthalmologic examinations which for the past 10 years have been included as part of the routine physical examination of the pupils at the Pennsylvania School for the Deaf in Philadelphia shows a higher incidence of refractive errors in this group of handicapped children than has been reported for hearing children of a comparable age group.

During this 10-year period 960 children have been examined and treated as the need arose by ophthalmologists in a weekly clinic held at the school infirmary.

At the time of admission to the school the visual acuity of each child was determined by the use of the illiterate "E" chart, based on the Snellen test sizes. It has been found that a more accurate determination of the visual acuity was obtained by use of this chart, since many of these children either are unable to talk or do not know the alphabet. The younger children were taught the use of this chart in the classroom before coming to the clinic for examination.

After the visual acuity was determined, each child was given a complete external examination of the eyes, as well as an ophthalmoscopic examination. On the basis of the findings it was decided whether a refraction should be done. Persons under 16 years of age were examined under atropine cycloplegia,[1] and those over 16, under homatropine cycloplegia.[2] Every child with visual acuity of less than 6/6 had refraction. Many children had 6/6 vision, but it was noted that the fundus in many was best visualized with a +3 D. or +4 D. lens. These children were given refraction under cycloplegia, and it was found that glasses materially improved their work in the classroom. In addition, children who presented strabismus or complained of eyestrain were treated in a similar manner.

After the initial examination and treatment, each child's eyes were rechecked at least every two years. Children who were myopic or presented some pathological condition, such as pigmentary degeneration of the retina (retinitis pigmentosa), of which we had 23 cases, were seen more frequently.

The number and percentage of refractive errors in boys and girls are shown in Table 1.

Presented as thesis in partial fulfilment of the requirements for Master of Medical Science in Ophthalmology, Graduate School of Medicine, University of Pennsylvania.

1. For atropine sulfate cycloplegia, a 0.5% solution for children up to 12 years of age and a 1% solution for those between 12 and 16 years of age are used. One drop is instilled in each eye three times a day for two days, plus 1 drop in each eye on the morning of refraction. Dark glasses are worn.

2. For homatropine hydrobromide cycloplegia, a 2% solution is used. The evening before refraction 1 drop is instilled into each eye. The next day, two hours before refraction, 1 drop is instilled into each eye every 10 minutes for one hour. Dark glasses are worn.

It is interesting to note that 433 children, or 45.5%, required glasses. This is a slightly higher figure than Braly [3] found at the New Jersey School for the Deaf at Trenton, in examination of 422 deaf children. He showed that 38% of the deaf children had defective vision, as compared with 22% of hearing children in the public schools. A recent survey in the Philadelphia public schools, reported last spring at the Philadelphia County Medical Postgraduate Institute,[4] revealed that 15% of the pupils had varying degrees of defective vision. This wide difference in the percentage of visual defects in deaf and in hearing children might be explained by the fact that only those children with defective vision, as determined by the Snellen eye chart, were sent to an ophthalmologist after examination in the public schools, whereas every child at the Pennsylvania School for the Deaf had an ophthalmologic examination.

TABLE 1.—*Refractive Errors in Boys and Girls*

	Without Glasses		With Glasses		
	No.	Per Cent	No.	Per Cent	Total
Boys	322	58.0	233	42.0	555
Girls	205	51.0	200	49.0	405
Total	527	54.5	433	45.5	960

TABLE 2.—*Analysis of Refractive Errors in Various Types of Deafness*

Type of Deafness	Cases		Per Cent Without Glasses	Per Cent With Glasses	Per Cent with Glasses with Compound Hyperopic Astigmatism
	No.	Per Cent			
Acquired deafness	342	36	55	45	76
Congenital deafness	488	51	53	47	76
Cause of deafness unknown	130	13	63	37	75

There were 342 children (36%) with acquired, as contrasted with 488 children (51%) with congenital, deafness. In the third group, with deafness of unknown cause, there were 130 children (13%). In the group with acquired deafness 45% needed glasses; in the group with congenital deafness, 47%, and in the group with deafness of unknown cause, 37%.

Other figures are not very significant because of the small number of cases in each group. A far greater number of cases than those analyzed in this paper would have to be tabulated in order to determine whether it is correct that in the groups with acquired and congenital deafness more boys than girls showed compound myopic astigmatism and more girls than boys showed mixed astigmatism.

3. Braly, K. W.: A Study of Defective Vision Among Deaf Children, Am. Ann. Deaf **83**:192-193 (March) 1938.

4. Weaver, R. H.: Early Recognition of Physical Defects, Philadelphia Med. **46**:1515-1519 (July 7) 1951.

Brown [5] calculated and tabulated the net hyperopia or myopia in over 1,000 strabismic eyes and 15,000 nonstrabismic eyes examined under atropine cycloplegia. His study revealed the following data [6]:

1. The amount of hyperopia present in the strabismic eye in excess of that in the nonstrabismic eye averages over +3.00 D. up to the age of 25 years.

TABLE 3.—*Percentage Analysis of Refractive Errors in Deafness*

		Acquired	Congenital	Cause Unknown
Hyperopia	B*	2.44	5.83	0.00
	A	1.95	5.23	0.00
	G	1.39	4.64	0.00
Compound hyperopic astigmatism	B	78.05	77.50	82.76
	A	75.97	75.79	72.96
	G	73.61	74.07	63.16
Myopia	B	0.00	2.50	6.90
	A	4.54	1.71	8.72
	G	9.72	0.92	10.52
Compound myopic astigmatism	B	13.41	10.00	3.41
	A	9.74	9.63	9.60
	G	5.56	9.26	15.79
Mixed astigmatism	B	6.10	4.17	6.93
	A	7.79	7.64	8.72
	G	9.72	11.11	10.53

* B, A, and G indicate percentages for boys, average percentages, and percentages for girls, respectively.

TABLE 4.—*Comparative Study of Average Net Refraction in Hearing and in Deaf Children and in Hearing Children with Strabismus*

	Average Net Refraction in Nonstrabismic Eyes (Brown [5])			Average Net Refraction in Deaf Children (This Series)			Average Net Refraction in Hearing Children with Strabismus (Brown [5])		
Age, Yr.	No. of Computations	Type	Refraction, D.	No. of Computations	Type	Refraction, D.	No. of Computations	Type	Refraction, D.
5	40	Hyperopia	1.45	58	Hyperopia	4.10	146	Hyperopia	3.79
6	84	Hyperopia	1.82	98	Hyperopia	2.39	111	Hyperopia	3.86
7	446	Hyperopia	2.64	110	Hyperopia	2.91	405	Hyperopia	3.92
8	527	Hyperopia	2.14	132	Hyperopia	1.99	372	Hyperopia	2.99
9	495	Hyperopia	0.21	109	Hyperopia	2.66	307	Hyperopia	3.45
10	503	Hyperopia	0.28	118	Hyperopia	2.16	397	Hyperopia	3.18
11	585	Hyperopia	0.05	112	Hyperopia	1.62	288	Hyperopia	4.49
12	605	Hyperopia	0.65	120	Hyperopia	1.96	328	Hyperopia	2.64
13	544	Myopia	0.88	138	Hyperopia	1.33	329	Hyperopia	1.78
14	434	Myopia	1.63	142	Hyperopia	1.67	278	Hyperopia	1.19
15	403	Myopia	1.68	111	Hyperopia	1.41	269	Hyperopia	1.12
16	490	Myopia	1.51	117	Hyperopia	0.88	142	Hyperopia	1.97
17	478	Myopia	1.27	80	Hyperopia	0.93	125	Hyperopia	1.90
18	385	Myopia	1.48	85	Hyperopia	1.21	96	Hyepropia	2.15
19	377	Myopia	1.32	53	Hyperopia	0.11	79	Hyperopia	1.82
20	354	Myopia	1.60	34	Hyperopia	1.36	57	Hyperopia	1.54

5. Brown, E. V. L.: Comparison of Refraction of Strabismic Eyes with That of Nonstrabismic Eyes from Birth to the Twenty-Fifth Year, Arch. Ophth. **44**:357-361 (Sept.) 1950.

6. When astigmatism was present, the refraction of the meridian of greatest curvature was added to that of the least curvature; the sum was divided by 2, and the mean was recorded as the refraction of the eye. Thus, with the vertical axis showing +2.00 D, and the horizontal axis +4.00 D, the mean, +3.00 D, was recorded as the refraction of the eye.

2. The strabismic eye loses much of its early hyperopia—"undergoes emmetropization"—and even moves a bit over into the myopic side, if anything, before the age of 25.

3. The change comes after the 11th year in the strabismic eye, whereas a marked decrease of hyperopia occurs in the nonstrabismic eye right after the 7th year.

4. The rate of decrease of the hyperopia is much slower in the strabismic than in the nonstrabismic eye.

Because of the small number of deaf subjects under 4 years and above 20 years of age in this study, only the figures for children from 5 to 20 years are presented.

While the amount of hyperopia in the deaf children is not as great as in the strabismic children, it is higher than in the nonstrabismic children. The decrease in the amount of hyperopia in the deaf children follows closely that of strabismic

TABLE 5.—*Ocular Pathological Defects*

	Acquired Deafness		Congenital Deafness		Deafness, Cause Unknown	
	Boys	Girls	Boys	Girls	Boys	Girls
Strabismus						
Convergent	3	6	4	4	..	..
Alternate convergent	1	2	2	2	..	..
Divergent	..	..	..	..	..	..
Alternate divergent	..	..	2	..	..	..
Absence of external rectus muscles	..	..	..	1	..	..
Bilateral coloboma of iris, lens, and choroid	1	1	..	..	..	..
Persistent hyaloid artery	..	..	1	..	..	..
Keratitis	5	1	..	..	..	..
Pigmentary degeneration of retina	2	1	13	6	1	..
Chronic dacryocystitis	2	..	..	..	..	..
Macular degeneration	..	1	..	2	..	..
Ptosis	..	..	1	1	..	..
Laurence-Moon-Biedl syndrome	..	..	..	1	..	..
Bilateral guttate choroiditis	1	..	..	..	..	..
Recklinghausen disease	1	..	..	..	..	..
Epicanthus	..	..	2	2	..	..
Posterior polar cataract	1	..	..	..	..	..
Total	17	12	25	9	1	0

children. One might hypothesize that these deaf children have congenital anomalies aside from, or coordinated with, their deafness, and so possibly have a marked delay in their developmental processes, including the growth changes, which are found in "normal" children.

Pathological conditions of the eyes in this series of 960 children were found to be as presented in Table 5.

No particular significance was noted as compared with the hearing child, with the exception of pigmentary degeneration of the retina, which has already been correlated with the deaf child. Shoemaker,[7] at the time he was ophthalmologist at the Pennsylvania School for the Deaf in Philadelphia, published a monograph on retinitis pigmentosa which represented a report of 17 children with this disease in attendance at the school. He found that this pathological condition was congenital, however late its manifestations came to light. Several of the patients with this disorder in my study were brother and sister.

7. Shoemaker, W. T.: Retinitis Pigmentosa, J. B. Lippincott Company, 1909.

In the course of this study at the Pennsylvania School for the Deaf, letters were sent to 68 similar schools for the deaf in the United States. The response was most interesting and enlightening. Most of the replies expressed interest, although many of the schools apparently did not have a similar program. Many of the schools gave a routine ocular examination at the time of admission. In several schools a child was given an ophthalmologic examination if he or she complained or if the teacher noticed some difficulty. Some of the results are noted in Table 6.[8]

TABLE 6.—*Percentage of Defective Vision Found in Several Schools for the Deaf in the United States*

New Mexico	49%	
Mississippi	15%	
California	45%	
Pennsylvania (Scranton)	11%	
Nebraska	22%	
New Jersey	38%	
Illinois	32%	(Boys 64%) (Girls 36%)

SUMMARY

One may emphasize the following points:

1. The incidence of refractive errors is higher in the deaf than in the hearing child.

2. In the deaf the amount of hyperopia follows the pattern of the strabismic rather than of the nonstrabismic child.

3. Every child at the time of admission to a school for the deaf should be given a complete ophthalmologic examination as part of a routine physical examination, so that an already existent ametropia may be corrected as soon as possible.

4. During his school years periodic ophthalmologic examinations should be done at regular intervals in order that the child may be helped to maintain his best possible visual efficiency.

2018 Pine St. (3).

Dr. Grace Nachod helped in the eye clinic.

Dr. Brown has permitted me to use his figures in this paper, so that the net refraction in the deaf group might be correlated.

8. Personal communications from private boarding schools for the deaf in the United States.

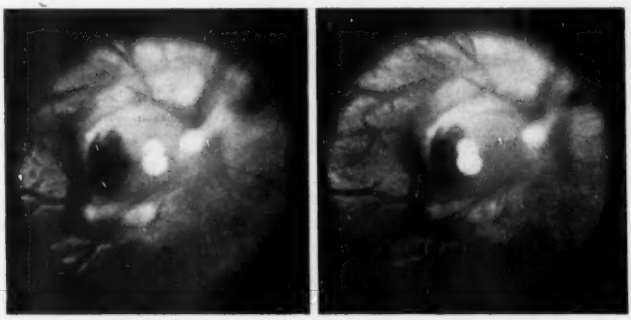
CONGENITAL PREPAPILLARY CYST

PAUL TOWER, M.D.
LOS ANGELES

CYSTIC masses at the surface of the optic papilla have frequently been described. But a congenital prepapillary cyst extending far into the retina, and lacking many of the characteristic diagnostic signs, may be interesting enough to warrant a brief report.

REPORT OF A CASE

R. S. L., a white boy 9 years of age, had had a normal birth and presented no history of congenital anomaly or ocular disease in the immediate family, At the age of 1 year a convergence of about 25 degrees was noted in the right eye, together with a congenital defect in the ocular fundus; no exact diagnosis was made. At the age of 5 years esotropia had increased to 35 degrees, and a congenital anomaly involving the optic disk was recognized.



Stereoscopic photographs of the right fundus of a 9-year-old boy. The site of the disk is covered by an elevated mass, which is clearly outlined by a deep shadow alongside its temporal margin. A remnant of Cloquet's canal is visible nasally.

At the age of 9 years the boy was referred with a tentative diagnosis of malignant tumor in the right eye. Vision in the left eye was 20/20, while in the right eye it amounted only to counting of fingers at 3 ft. (90 cm.). The cornea, iris, lens, and media were clear and normal in both eyes; the pupils were equal and reacted well to light and in accommodation. The convergent squint of the right eye had remained at 35 degrees.

Ophthalmoscopic examination showed that the fundus of the left eye was normal in every respect. In the right fundus there appeared an ovoid cystic mass, of grayish color, elevated about 4 D. above the level of the papilla. The optic disk was completely hidden by the growth, which on the temporal side extended far into the retina. The retinal vessels emerged at the nasal side of the mass; otherwise the vascular pattern was essentially normal. The larger branches followed mainly the contour of the cyst; some of them, however, could be seen to dip down from its temporal edge before proceeding toward the macular area. Some of the smaller branches pursued an uninterrupted course across the prominent growth, giving off capillary vessels which spread

over its surface and connected with a large dark area close to the temporal border of the cyst. This area was at first believed to be a hemorrhage, but it did not change its size or position during two years of observation.

Except for this blotch, no pigment deposits could be discerned on the surface of the cystic mass. Its margins, however, were rather well defined, especially on the temporal side, by a wide, dark shadow. The rest of the tumor was almost completely surrounded by an irregular zone of atrophy, deep to the retinal vessels, and most pronounced in the lower portion, where irregular flecks of light and dark pigmentation were observed. Close to the nasal border of the cyst a remnant of Cloquet's canal was present, which could be followed anteriorly far into the vitreous; the structure presented the classic dumbbell shape, but no vestige of the hyaloid artery could be detected, not even at the posterior capsule of the lens, during slit-lamp examination.

With movement of the eye the cystic growth showed a slight shimmying motion, and the proximal portion of the superior temporal vessels, otherwise hidden from view, was momentarily exposed. Observations extending over a period of years failed to demonstrate any changes in size or structure of the cyst or of any other part of the ocular fundus.

Roentgenographic studies gave no evidence of soft tissue, osseous densities, or any other abnormality in the right orbital area. The optic foramen was not enlarged; it was clearly demarcated and without signs of osteosclerosis. No congenital abnormality was found anywhere else in the body.

COMMENT

Reports of cystic masses at the intraocular surface of the papilla go back to the early days of ophthalmoscopic observation. At first, the lesion was traced to the Cysticercus,[1] but a congenital origin was soon suspected.[2] Hyaloid cysts have been classified as pseudotumors [3]; they assume a variety of shapes [4] but often form small, round, pearly-gray bodies, situated upon the disk.[5] It should be stressed that the cystic character of these masses becomes apparent only upon binocular observation, and that confirmation through microscopic examination is still lacking.[6] Often only part of the disk is covered by the growth, and, except for moderate enlargement of the blind spot, vision in the affected eye is unimpaired.[7] There are cases on record in which congenital prepapillary cyst is not accompanied by muscle imbalance.[8] Thus it has been rightly concluded that amblyopia and squint are not necessarily diagnostic criteria of congenital prepapillary cyst.[9] Apparently, size of cyst and degree of visual impairment are not directly related, and in one instance a mass, covering only one-third of the disk, resulted in almost complete loss of vision in that eye.[10]

1. Liebreich, R.: Cysticercus im Glaskörper, von Graefes Arch. Ophth. **1**:343-346, 1855.
2. Kollock, C. W.: A Peculiar Growth of the Optic Papilla, M. News **49**:456 (Oct. 23) 1886.
3. Purtscher, E.: Peculiar Tumor of the Optic Nerve Head, Ztschr. Augenh. **88**:217-224 (Feb.) 1936.
4. Parsons, J. H.: The Pathology of the Eye, London, Hodder & Stoughton, 1908, Vol. 3, Pt. 1, p. 858.
5. Duke-Elder, W. S.: Text-Book of Ophthalmology, Vol. 2, St. Louis, C. V. Mosby Company, 1938, p. 1378.
6. Lloyd, R. I.: Variations in the Development and Regression of Bergmeister's Papilla and the Hyaloid Artery, Tr. Am. Ophth. Soc. **38**:326-332, 1940.
7. Levitt, J. M., and Lloyd, R. I.: Congenital Prepapillary Cyst Containing a Moving Vascular Loop, Am. J. Ophth. **22**:760-764 (July) 1939.
8. Agatston, S. A.: Congenital Cyst of the Optic Nerve, Am. J. Ophth. **27**:278-279 (March) 1944.
9. François, J.: Pre-Papillary Cyst Developed from Remnants of the Hyaloid Artery, Brit. J. Ophth. **34**:365-368 (June) 1950.
10. Hilgartner, H. L.: Benign Cyst of the Optic Disk, Am. J. Ophth. **23**:186-187 (Feb.) 1940.

Congenital prepapillary cyst remains stationary and does not result in progressive deterioration of vision.[9] These characteristics permit differentiation from the rare prepapillary cyst due to glioma of the optic nerve [11] or other types of acquired cysts of the optic disk.[12] As a further diagnostic sign, the concomitant presence of other congenital anomalies has been postulated, but cannot be considered strictly pathognomonic. Blood vessels crossing the growth may give the impression of detachment of the retina by a semisolid or cystic mass; but in cases of this type the finding of remnants of Cloquet's canal on the capsule of the posterior lens, even though not accompanied by traces of the hyaloid artery at the disk, has been regarded as decisive.[13] It may at times be difficult to distinguish a prepapillary cyst from a persistent Bergmeister papilla, occasionally observed without any vestige of the hyaloid artery [14] or from an epipapillary membrane,[15] which, however, is ordinarily not accompanied by visual symptoms.[16]

Differential diagnosis always calls for a diligent search of the retina and other deep structures of the eye for old or recent inflammatory lesions, in the presence of which the congenital character of the growth becomes doubtful. Differentiation from syphilitic or tuberculous granuloma must be based on specific tests, and roentgenologic studies may be required to eliminate the possible presence of an intraocular tumor.

The case reported here is interesting in several respects. A congenital lesion is suggested by the fact that visual impairment, as well as the size and structure of the mass, remained stationary throughout the period of observation. Furthermore, amblyopia and squint were present, and a remnant of Cloquet's canal appeared at the classic site. There was no indication of old or recent inflammation, or of a tumor process involving the globe, orbit, or deep cranial structures. Most likely the prepapillary cyst represents the posterior portion of Cloquet's canal, which has been tremendously dilated, and not only obscures the entire papilla but also covers a considerable part of the adjacent retina. However, the large pigmented spot on the surface of the mass (hemorrhage?), as well as the atrophic zone almost completely surrounding the prepapillary cyst, remains unexplained.

610 South Broadway (14).

11. Verhoeff, F. H.: Primary Intraneural Tumors (Gliomas) of the Optic Nerve, Arch. Ophth. **51**:120-140 (March); 239-254 (May) 1922.

12. Levine, J.: Acquired Cyst of the Optic Disk, Arch. Ophth. **8**:209-217 (Aug.) 1932.

13. Yudkin, A. M.: Congenital Tumor Mass at the Edge of the Optic Disk, Arch. Ophth. **55**:364-366 (July) 1926.

14. Mann, I.: Developmental Abnormalities of the Eye, New York, Cambridge University Press, 1937, p. 132.

15. Straub, W.: Beitrag zur Klinik der persistierenden Glaskörperarterie, Ophthalmologica **121**:194-200 (April) 1951.

16. Bedell, A. J.: Anomalies of the Fundus Oculi, Pennsylvania M. J. **51**:40-43 (Oct.) 1947.

POSSIBLE ROLE OF PROPRIOCEPTION IN THE EXTRAOCULAR MUSCLES

ELEK LUDVIGH, Ph.D.
DETROIT

THE FINDING by Daniel,[1] confirmed by Cooper and Daniel[2] and Sunderland,[3] of muscle spindles in the extraocular muscles of the human eye, and also in the eyes of other animals with mobile eyes, raises the question of the possible function of these end-organs. It has been shown by Irvine and Ludvigh[4] that the human eye appears to have little, if any, position sense. These authors concluded:

> The proprioceptive sense in the extra-ocular muscles has been tested for and found lacking by application of the usual criteria, namely: (1) histologic and anatomic evidence, (2) vibration sense, (3) myotatic reflexes and (4) position sense. For the possibility that ocular proprioceptive nerves not mediating position, operating at a low level, exist there is no physiologic evidence.

The very existence of muscle spindles in the human eye completely invalidates the first line of evidence quoted above. Criteria 2, 3, and 4 and the evidence supporting their absence in the extraocular muscles remain unaffected by the finding of muscle spindles. Yet the presence of muscle spindles in the extraocular muscles would certainly suggest that these spindles perform a function similar or analogous to that which they perform in skeletal muscle. Since the classic view is that muscle spindles in skeletal muscle perform, at least in part, the function of mediating position sense, it seems worth while to reexamine the problem of the position sense of the eye.

Experimental evidence has previously been advanced[4] to demonstrate that (1) persons with paralyzed eye muscles may be unaware of the position of their eyes; (2) persons with nystagmus may not know that their eyes are moving; (3) normal persons with nystagmus induced by vestibular stimulation may believe that their eyes are stationary and that the environment is moving, and (4) normal persons whose eyes are moved passively by grasping of the anesthetized conjunctiva with forceps are unaware of the movement. However, it might be argued that these experiments were all conducted under somewhat abnormal conditions in that the subject tested either had a defect of ocular motility, or the eye was anesthetized, or

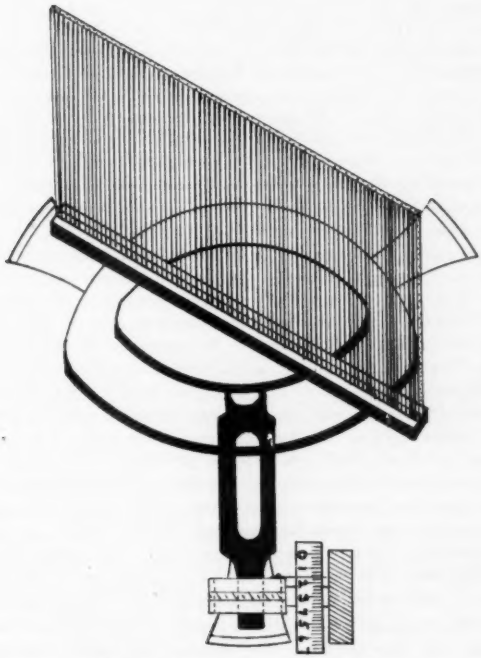
From the Kresge Eye Institute.

1. Daniel, P.: Spiral Nerve Endings in Extrinsic Eye Muscles of Man, J. Anat. **80**:189, 1946.

2. Cooper, S., and Daniel, P.: Muscle Spindles in Human Extrinsic Eye Muscles, Brain **72**:1, 1949.

3. Sunderland, S.: A Preliminary Note on the Presence of Neuromuscular Spindles in Extrinsic Ocular Muscles in Man, Anat. Rec. **103**:561, 1949.

4. Irvine, S. R., and Ludvigh, E. J.: Is Ocular Proprioceptive Sense Concerned in Vision? Arch. Ophth. **15**:1037, 1936.



Sketch of rotating-mirror assembly.

in one way or another an abnormal and unphysiologic condition existed. Chavasse [5] suggested that the proprioceptive sense of the extraocular muscles is inhibited under exceptional conditions and that this accounts for the seeming lack of proprioception. The present paper describes experiments conducted in an effort to demonstrate the presence or absence of position sense in the extraocular muscles under conditions which are strictly physiologic.

METHOD OF INVESTIGATION

Since it was believed that if position sense were absent the subject would use any possible alternative clue to determine the position of the eyes, it was deemed advisable to minimize the number of such clues by keeping the apparatus as simple as possible; and, indeed, this was found to be necessary. A front-surface mirror, 5½ in. (14 cm.) high and 3½ in. (8.9 cm.) wide, was mounted on a turntable (Fig. 1). The turntable was rotated by adjustment of a lead screw which positioned an arm attached to the turntable. Spring loading was employed to reduce backlash. The subjects viewed a test object in the mirror, and rotation of the mirror produced apparent displacement of the test object. The equipment was calibrated by viewing a light source through a semitransparent mirror and observing the visual projection of this source on a screen located in the plane of the test object on which screen measurements of displacement were made. After calibration the front-surface mirror was substituted for the semitransparent mirror.[6] The seated observer placed his head in a headrest, consisting of a concavity for the chin and a button pressing against each side of the forehead. In an otherwise dark room the subject looked into the mirror and saw the test object situated at a distance of 1 meter. An artificial pupil was not employed. The test object consisted of a disk of light projected from the side opposite that from which the observer viewed it in order that reflections should be reduced. The diameter of the disk was 1 cm., and it thus subtended approximately 30 minutes of arc at the nodal point of the observer's eye. The "brightness" of the disk was 2.1 foot-candles (f.-c.) as measured by viewing it directly with a Macbeth illuminometer. This brightness level is ordinarily assumed to be well above the cone threshold.[7] The observer focused a small black dot subtending less than 3 minutes of arc at the nodal point of the eye. The dot was placed in the center of the bright disk. Owing to the rapid decrease of visual acuity from fovea to periphery,[8] the visibility of the black dot provided substantial evidence that the fovea was employed. Care was exercised to reduce stray light and reflections from the apparatus or other portions of the room. The edges of the mirror were obscured by a black screen, which was extended along the side of the observer's head to prevent him from viewing the light other than via the mirror. The headrest was adjusted so that in the illuminated dark room with the mirror in its zero, or neutral, position the test object as viewed by the right eye with the left eye covered appeared to be "straight ahead."

Mirror rotations providing displacements equivalent to the introduction of prisms of 2, 5, and 8 △, base in and base out, were presented. The observer, with the left eye occluded, closed his eyes. A displacement of the test object equivalent to 5 △ to the right was presented. The observer was now instructed to open his eyes and told, "Look at the test object. You are now looking to the right." This was immediately followed by a similar presentation to the left, and

5. Lyle, T. K.: Worth and Chavasse's Squint: The Binocular Reflexes and the Treatment of Strabismus, Philadelphia, Ed. 8, The Blakiston Company, 1950, p. 177.

6. If ordinary trial-case prisms or a back-surface mirror is used, the subject will employ the faint multiple reflections as clues to inform him of the position of the eyes. These clues may be used consciously and be reported, or they may be used without awareness of the fact, the observer not knowing the basis on which he is stating that his eyes have moved to the right or to the left.

7. Bartley, S. H.: Vision: A Study of Its Basis, New York, D. Van Nostrand Company, Inc., 1941, p. 186.

8. Ludvigh, E. J.: Extrafoveal Visual Acuity as Measured with Snellen Test-Letters, Am. J. Ophth. **24**:303, 1941.

this demonstration of right and left was made at intervals throughout the experiment. After such a demonstration, the eyes were again closed, and a displacement was produced at random, as determined by the chance selection of playing cards. The observer was instructed to open his eyes and was asked whether he thought he was looking to the right or to the left. If, as in most instances, he had no conviction as to the direction in which he was looking, he was, nevertheless, asked to make a statement one way or the other.

RESULTS AND COMMENT

The results of 100 observations taken at each displacement used for two observers are shown in the accompanying table. It may be observed from this table that a differential displacement of approximately 12 Δ (6 Δ right plus 6 Δ left), or 6 degrees, would produce approximately 75% correct judgments for both observers. When the apparatus was rotated about 90 degrees and an auxiliary front-surface mirror employed, it was found by an entirely analogous experiment that vertical motions of the eyes of approximately one-half the extent of the horizontal motions could be detected with equal reliability.

The results indicate that the eye has position sense, but that ocular movements substantially in excess of 6 degrees must occur for the observer to state with high

Percentage of Correct Judgments of Two Observers in Displacement Experiments

Displacement Right or Left, Δ	Correct Judgments, %	
	Observer A. H.	Observer E. N.
2	50	60
5	68	72
8	92	92

reliability whether the eye is directed to the right or to the left. As compared with the ability to distinguish the direction of the eyes relative to an object, this position sense is indeed gross. For example, it has been shown that an examiner objectively observing the subject's eye would with equal reliability detect the direction of motion in movements of one-tenth this amount [9] and that the subject moving his eye would, if permitted retinal clues, be able to detect a fraction of this fraction. Thus, it appears that the actual position of the eyes provides, at best, only relatively gross information as to where the eyes are.

The lack of position sensitivity of the eye is further emphasized by comparison with the accuracy of location of the hip joint, even on passive movement, where an angular change of 0.2 degree is perceptible.[10]

It may be observed that in this experiment no false clues were provided which might inhibit proprioception, and that the experimental situation was such as to encourage the use of proprioception for the determination of eye position. Even under these favorable conditions it appears that the proprioceptive sense cannot reliably furnish information adequate for determination of the position of the eye

9. Ludvigh, E. J.: Amount of Eye Movement Objectively Perceptible to the Unaided Eye, Am. J. Ophth. **32**:649, 1949.

10. Laidlaw, R. W., and Hamilton, M. A.: A Study of Thresholds in Apperception of Passive Movement Among Normal Control Subjects, Bull. Neurol. Inst. New York **6**:268, 1937.

to an accuracy of better than 10 degrees. Indeed, it seems likely that the position sense is not even furnishing this information, since the increased position sense obtained with vertical movements of the eyes lends support to the notion that sensations from the lids, and possibly also from the levator muscle, may provide approximate information as to the position of the eyes.

Under unfavorable conditions, such as those obtaining when false retinal clues are employed, the observer may be caused to "feel" that his eyes are in violent motion, even to the point of fatigue, when they are, in fact, stationary, as the following experiment shows: A semitransparent mirror is so placed that a light source may be viewed through the mirror, while the rest of the environment, which consists of a normally lighted room, is viewed as reflected in the mirror. The mirror can be rotated in either direction about a vertical axis by a reversible motor. The observer fixates the light through a tube, the purpose of which is to exclude most of the extreme peripheral stimuli, which, since they are not viewed in the mirror, might otherwise provide a stationary frame of reference. When the mirror is set in motion, first in one direction and then in another, some observers will see the light moving across the walls and windows of the room. Some, indeed, may set the hand-held tube in nystagmus-like motion, with a slow and fast component, in the effort to follow the light. Questioned as to whether they could keep up with the light if it were moved faster, they may respond that they could, or think they could, or they may volunteer that they think it would be fatiguing, when, as a matter of fact, objective observation of the eye shows that it is substantially stationary and no movement of the tube is necessary to keep the light centered. In this situation the observer may believe that his eyes are in active pursuit of the wandering object.

It is clear that in an experimental situation of this extreme simplicity the aforementioned result is more likely to be obtained with subjects who are unaware of the purpose of the experiment. It is true that in this demonstration the observer has been tricked and that the experiment presents him with a more unusual situation than does the presentation of the light in the dark room; nevertheless, even a relatively gross position sense should indicate that the eye is not moving through the 30 or 40 degrees that the displacement of the background on the retina suggests.

CONCLUSIONS

The conclusion to be drawn from the experiments described above, as well as from those previously described,[4] is that the muscle spindles in the extraocular muscles give rise to little, if any, acceptable information concerning the position of the eyes; indeed, the tendency of recent opinion seems to be that it is doubtful to what extent muscle spindles in skeletal muscle can mediate a knowledge of the position of the limbs. Thus, Gardner,[11] in discussing the investigations of Sarnoff and Arrowood[12] and McIntyre and Lloyd,[13] stated:

11. Gardner, E.: Physiology of Movable Joints, Physiol. Rev. **30**:127 (April) 1950.

12. Sarnoff, S. J., and Arrowood, J. G.: Differential Spinal Block: III. The Block of Cutaneous and Stretch Reflexes in the Presence of Unimpaired Position Sense, J. Neurophysiol. **10**:205, 1947.

13. McIntyre, A. K., and Lloyd, S. P. C.: Spinal Projection of Hindlimb Afferent Fibers, Federation Proc. **7**:79, 1948.

McIntyre and Lloyd found that Group I fibers from muscle ascend for but a relatively short distance in dorsal funiculi before ending, presumably by relay through the nucleus dorsalis. It would be interesting to know if a similar situation exists in man. If it does, either muscles and tendons do not contribute to the so-called muscle-joint-tendon sense, or they have a route to consciousness other than dorsal funiculi. Joint fibers do ascend in dorsal funiculi and perhaps form the major component of this sensory quality.

The position of the limbs may be known by articular sensitivity alone. The eye, however, lacks articular sensitivity, and the question then arises as to how ocular movements are controlled, considering the degree of speed and precision which they exhibit. In a subsequent paper, the hypothesis is advanced with supporting evidence that the chief function of the muscle spindles may be to provide a parametric feedback,[14] which alters the response of the muscle to motor stimulation by means of a mechanism similar to that which Gellhorn finds operative in skeletal muscle.[15]

14. Trimmer, J. D.: Response of Physical Systems, New York, John Wiley & Sons, Inc., 1950, p. 200.

15. Gellhorn, E.: Proprioception and the Motor Cortex, Brain **72**:56, 1949.

CONTROL OF OCULAR MOVEMENTS AND VISUAL INTERPRETATION OF ENVIRONMENT

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DETROIT

EVIDENCE [1] has been advanced that the eye lacks position sense; furthermore, evidence [2] has appeared that the muscle spindles found by Daniel [3] in the extraocular muscles do not effectively contribute to a position sense of the eye. Furthermore, in recent years substantial doubt has arisen as to whether muscles and tendons contribute to the position sense of skeletal muscle or whether this position sense is mediated chiefly or solely by the joint, or articular, sensitivity.[4] The problem thus arises as to how the individual controls his eyes and interprets the movement, or lack thereof, of environment when he is not consciously aware of the position of his eyes. It is with this problem that the present paper is concerned.

The classic explanation for the control of bodily movements, including eye movements, is by means of what has been characterized as the "proprioceptive-pyramidal circuit."[5]

The expression "feedback" has recently come into rather general use in describing the action of the proprioceptive-pyramidal circuit, and this term may well be preferred both as being shorter and as implying less knowledge concerning the nature of the mechanism involved. In modern terminology the carrying out of a motion such as moving the forearm until it makes a right angle with the upper arm might be described as follows: There is recorded somewhere or somehow in the cortex the desired proprioceptive neural pattern. There is received from the articular sense a definite pattern that is not the desired one. The difference between the desired and the received pattern is the error signal. This error signal produces a change in the innervation sent to the relevant muscles, with the result that the arm moves, thereby changing the articular pattern. This change in pattern, in turn, results in a change in the error signal, and the new innervation is sent out,

From the Kresge Eye Institute.

1. Irvine, S. R., and Ludvigh, E. J.: Is Ocular Proprioceptive Sense Concerned in Vision? Arch. Ophth. **15**:1037, 1936.

2. Ludvigh, E. J.: Possible Role of Proprioception in the Extraocular Muscles, A. M. A. Arch. Ophth., this issue.

3. Daniel, P.: Spiral Nerve Endings in Extrinsic Eye Muscles of Man, J. Anat. **80**:189, 1946.

4. Gardner, E.: Physiology of Movable Joints, Physiol. Rev. **30**:127, 1950. Sarnoff, S. J., and Arrowood, J. S.: Differential Spinal Block: III. Block of Cutaneous and Stretch Reflexes in the Presence of Unimpaired Position Sense, J. Neurophysiol. **10**:205, 1947. McIntyre, A. K., and Lloyd, D. P. C.: Spinal Projection of Hindlimb Afferent Fibers, Federation Proc. **7**:79, 1948.

5. Troland, L. T.: Principles of Psychophysiology, New York, D. Van Nostrand Company, Inc., 1932, Vol. 3, pp. 364, 362-363.

causing a further change in the position of the arm until the difference between the desired proprioceptive-neural pattern and the received proprioceptive pattern, in other words, the error signal, is, for our purposes, zero. At this point motion stops. Since the visual environment is ordinarily heterogeneous, movements of the eye will bring about a change in retinal and neural pattern even in the absence of any interoceptive sense. This is not, in general, true of skeletal limbs, in which motion would not result in change in neural pattern in the absence of interoceptive sense or skin sensitivity. In the instance of the eye, where evidence of the ineffectivity of the muscular sense in providing information as to position is perhaps somewhat more cogent than it is in skeletal muscle, and where articular sensitivity is nonexistent, it is tempting to resort to the hypothesis that the retina provides the necessary error signal in the form of retinal, or exteroceptive, feedback. However, the hypothesis of exteroceptive feedback for the control of an ocular motion, such as a change of fixation from one point to another, although on the surface attractive, must be far from adequate. As has been pointed out in a previous paper,[1] it is quite unlikely that the eyes operate in so simple a manner, since entire large excursions of several degrees may be initiated and completed before there is time for any error signal of either interoceptive or exteroceptive nature to become effective.

Let us consider in somewhat more detail the phenomena which occur when the eye performs two of its commoner functions. One of these is a change of fixation, the fovea abandoning one point of fixation and picking up another point. The second is one in which, the fovea having been directed toward a fixed point, a moving object appears at that fixed point traveling at constant velocity and the eye pursues this moving object. In the former situation the eye is subjected to a unit-step stimulus, while in the latter it is subjected to a unit-velocity step stimulus. Both types of stimulus or input to the eye and the response of the eye thereto appear to have been first investigated quantitatively by Dodge,[6] although there had been previous investigators in this field. Dodge described both the slight errors on change of fixation, which in modern terminology would be called overshoot, and the lag of the eye in following a steady velocity, which would now be called the velocity error constant.[7]

The experimental situation employing the unit-step stimulus may be described as follows: While the subject is fixating one light, another light appears in the field situated, say, 20 degrees to the right. The subject changes fixation to the second light. Dodge finds a lag of approximately 0.2 second, after which the eye starts moving and travels through 20 degrees, or 1,200 minutes, of arc in approximately 0.05 second. There may be slight overshoot or undershoot, particularly for large excursions, but the performance, in general, is about as accurate as extrafoveal visual acuity will permit. The problem here is how the initial innervation can produce the surprising velocity and accuracy of eye movement which results.

6. Dodge, R.: Five Types of Eye Movements in the Horizontal Meridian Plane of the Field of Regard, Am. J. Physiol. **8**:307, 1903.

7. James, H. M., and Others, Editors: Theory of Servo-Mechanisms, Office of Scientific Research and Development, National Defense Research Committee, New York, McGraw-Hill Book Company, Inc., 1947, p. 26. Hazen, H. L.: Theory of Servo-Mechanisms, J. Franklin Inst., 1934, p. 218.

The experimental situation employing the unit-velocity step stimulus is as follows: While the subject is fixating one light, another stroboscopically flashing light suddenly appears at the point of fixation, moving at a constant angular velocity. The eye pursues the moving light. I have found that with a similar time delay of approximately 0.2 second angular velocities of 14 degrees per second are being pursued with substantial accuracy 0.2 second later. The problem here is how the initial innervation can produce the accurate velocity of eye movement necessary for successful pursuit. There is not time for exteroceptive feedback to influence the response to either the unit-step or the unit-velocity step stimulus, since it required 0.2 second (voluntary changes of fixation may take as long as 0.5 second) [8] from the time when the displacement on the retina occurred to the time when the effect of the error signal could become manifest in a changed velocity, or acceleration, or higher derivative, of eye motion. This reasoning does not necessarily apply to fusional movements which subserve unification.[9] The effective stimulus for such movements is disparateness; furthermore, it is likely that one of the retinal images must be consciously perceived.[10] These fusional movements are relatively very slow,[11] and fusional movements of even small amplitude require from 0.5 to 2.5 second for completion. In view of the marked differences between fusional movements and those previously discussed, it is possible that fusional movements are mediated by exteroceptive feedback, and this possibility constitutes an interesting subject for investigation.

The view previously advanced, "that proprioceptive sense, if extant in the extraocular muscles, plays no role in projection, stereopsis or the interpretation of motion on the retina" [1] remains cogent. However, it is extremely helpful to our understanding of ocular motions to have some form of proprioception available. If proprioception were not available in any form, slight variations, of the order of 1% or less, in the efficiency of the extraocular muscles would produce relatively serious errors in the positioning of the eye. Suppose that a sudden change of fixation to, say, 20 degrees left is called for. An innervation is sent out which was previously adequate to accomplish this movement, but it is assumed that the relative efficiencies of the various muscles involved have been altered by a different position of the eye, differences in tonus, metabolism, or other factors and that, as a consequence, the eye moves only 18 degrees. The Snellen acuity is now only 20/100 for the desired object of fixation,[12] and, furthermore, the 2-degree discrepancy does not appear as an error signal; rather, it is interpreted as a movement of the object. Now a second movement of change of fixation may occur and fixation may be achieved. However, the characteristics of the system have not been altered, and if the entire procedure were to be repeated, similar gross errors would occur. We know that under normal conditions the eye does not make such errors. The explanation of why these errors in fixation do not occur may be in terms of the muscle spindles

8. Lord, M. P., and Wright, W. D.: Small Voluntary Flicking and Following Eye Movements, Nature, London **163**:803, 1949.

9. Verhoeff, F. H.: A New Theory of Binocular Vision, Arch. Ophth. **13**:151, 1935.

10. Cogan, D. G.: Neurology of the Ocular Muscles, Springfield, Ill., Charles C Thomas, Publisher, 1948, p. 93.

11. van Heuven, J. A.: La Vision binoculaire, Arch. Neurol. de Physiol. **11**:83, 1926.

12. Ludvigh, E. J.: Extrafoveal Visual Acuity as Measured with Snellen Test-Letters, Am. J. Ophth. **24**:303, 1941.

found by Daniel. If the end-organs discovered by Daniel are demonstrated to have a true proprioceptive function, then the output of these end-organs may alter tone or some other parameter of the oculomotor system and thus provide what would now be called parametric feedback.[13] Conceivably, the fixation tremor[14] of the eye may provide parametric excitation.[15] The presence of nonlinear physiological elements is almost certain, and these can provide stability. The apparent absence of any organs capable even of providing data for parametric feedback has been a chief stumbling block in our understanding of the control of ocular movements.

The general manner in which movements of change of fixation and steady angular pursuit velocity could be attained may be as follows: A perceived distance from the fovea or a perceived velocity results in a definite and fixed timed sequence of innervation. Of this the individual is aware, and upon this innervation he bases his sense of the position of his eyes, correct or incorrect. However, depending upon the position of the eyes and the tonus and efficiency of the various extraocular muscles, this innervation, before it becomes effective or as it becomes effective, is modified by proprioceptive impulses from the extraocular muscles in such a manner that the innervation does, indeed, carry out the indicated movement. The mechanism by which such modification can be brought about is not known, but it has been shown by Gellhorn[16] that such a mechanism does exist for skeletal muscle. Furthermore, this mechanism is mediated chiefly by muscle and tendon sense and little, if at all, by articular sensitivity. Gellhorn states[16]:

> Taking the experimental results of this and the preceding paper into account, it may be said that proprioceptive impulses increase the responsiveness to cortical stimulation of those muscles in which the impulses originate as a result of passive stretching and active tension, and that the effect is directly related to these two factors.

The effect would appear to be ample to account for the efficient modification of the original innervation. As Gellhorn stated,[16]

> The magnitude of this intensification is considerable since subthreshold cortical stimulation may be made effective by bringing proprioceptive impulses into play whereas often even a considerable increase in stimulus intensity fails to cause the same motor effect in the absence of such facilitatory proprioceptive impulses.

A tentative schematic diagram for the qualitative explanation of various normal and abnormal ocular movements and the accompanying perception of movement, or lack thereof, of the eyes and the environment is given in the accompanying Figure. An essential point in interpreting the subject's perception is that he is subjectively unaware of the processes occurring to the right of the dashed vertical line in this Figure. In terms of this diagram, a normal eye movement of change of fixation may be described as follows: An impulse to conjugate innervation for, say, 10 degrees eyes right is sent out from the conjugate innervation center to the motor system of each eye. At the same time there is sent to the functional region, designated space representation, impulses indicating the nature of the impulses sent to the

13. Trimmer, J. D.: Response of Physical Systems, New York, John Wiley & Sons, Inc., 1950, p. 200.

14. Adler, F. H., and Fliegelman, M.: Influence of Fixation on the Visual Acuity, Arch. Ophth. **12**:475, 1934. Riggs, L. A., and Ratliff, F.: Coordination of the Eyes in Maintaining Fixation, Am. Psychologist **5**:260, 1950.

15. Minorsky, N.: On Parametric Excitation, J. Franklin Inst. **240**:25, 1945.

16. Gellhorn, E.: Proprioception and the Motor Cortex, Brain **72**:35, 1949.

motor system. The innervation sent to the motor system arrives at a parametric adjustment center for each eye. Now, owing to the position of the eyes, the tonus of the individual extraocular muscles, and the fixation tremor, varying proprioceptive impulses are continually being generated. The parametric center continually adjusts to these impulses, with the result that either the innervation received is modified or impulses are sent altering the response characteristics of the appropriate muscle in such manner that, for the position of the eye and the tonus of the various extraocular muscles involved, the muscles exert the force necessary to move the eye substantially 10 degrees. The resultant movement of the eyes brings about a displacement of the images on the retina. Retinal feedback now occurs, and nerve impulses are transmitted to the region of spatial representation. When impulses received from the retina are such as to indicate that the ocular movement agrees substantially in magnitude and direction with the expected magnitude and direction

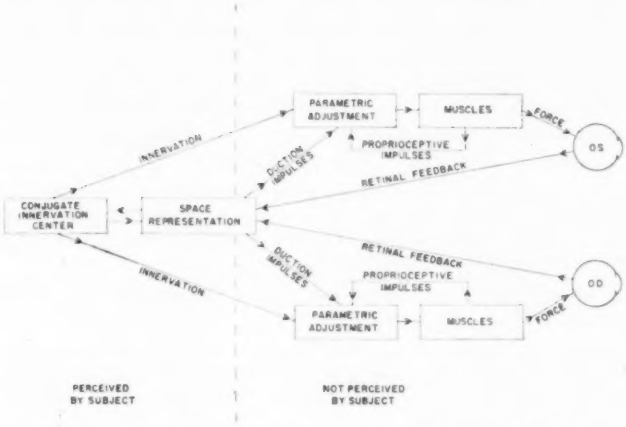

Diagram for qualitative explanation of various normal and abnormal ocular movements and the accompanying perception of movement, or lack thereof.

sent down by conjugate innervation, there will be no apparent movement of the environment. Because the original conjugate impulse is necessarily based on information received from a region of the retina where visual acuity is relatively low, the resulting movement frequently is inaccurate by ½ degree or so. There is still no apparent movement of the environment because the image displacement on the retina corresponds to the innervation sent out, even though the latter is incorrect for the purpose of achieving fixation. Now, after a definite delay time of the order of 0.2 second, a corrective conjugate innervation is sent out which results in a second movement of the eye. The second movement is more precise than the first, since the visual acuity in the immediate vicinity of the fovea is much higher than that which was operative in initiating the first movement. The second movement, too, is not accompanied by any conscious movement of the environment. On the basis of this hypothesis, a definite innervation sequence always follows a specific extrafoveal position, regardless of the position of the eyes, the state of tonus

of the individual extraocular muscles, or other factors. It is the repeated operation of the retinal feedback system which brings about discrete corrective movements occurring on change of fixation—not inaccuracies of motor response, as has previously been suggested.

Next, let us consider a quite different state of affairs which occurs when eye movement is involuntary. Suppose, with both eyes open, a 2-Δ prism is dropped, base up, before the right eye. The image moves off the fovea of the right eye, and conscious diplopia results. Unlike the situation involved in voluntary fixation, there is no rapid corrective movement, but the two images gradually move together. This merging of the images is entirely involuntary. Since, as has been previously pointed out, one image must be consciously perceived, the innervation must arise cortically. However, because of the slow speed, gradually decreasing velocity, and involuntary nature of this type of corrective movement, it appears that the innervation arises from the space-representation region and the eyes are controlled by retinal feedback. Motion of the object during the process of fusion is perceived but the subject does not know that his eyes are moving and, a fortiori, he does not know which eye is moving.

Next, let us consider the classic situation in which the eye is displaced mechanically. Under this condition, no change of innervation is sent to the eyes, and hence no change in impulses to the space-representation region; but impulses arise from the retina itself, since the retina is displaced behind the image. These impulses result in the perception of motion in the environment in the absence of balancing impulses coming from the conjugate innervation center.

Another instance in which the impulses received by the space-representation region do not conform with the retinal feedback occurs in persons with paresis or nystagmus of recent onset. In both conditions motion of the environment is perceived. Let us consider the instance of partial paresis of a muscle. (It is interesting to note that theoretically the defect must be relatively severe. Minor variations in strength of the individual extraocular muscles could be taken care of by an appropriate adjustment of the parameter relating strength of innervation to muscle output.) Let us assume that the muscular deficiency is so great that even the increased stimulus provided by the compensating system is inadequate. Then, when an amount of innervation which under normal conditions would produce a movement of 10 degrees eyes right is sent to the motor system and equivalent impulses are sent to the space-representation center, an eye movement results which is less than 10 degrees, and the impulses from the retina are correspondingly also less than they would have been for a 10-degree eye movement. Motion of the environment is, therefore, perceived. Note how this differs from the lack of motion of the environment when the cortical innervation was insufficient because of conscious underestimation of the distance it was desired to move the eyes.

When the paresis persists for a relatively long time, the individual may learn to fixate and to interpret the environment by substantially disregarding the conjugate innervation sent to the space-representation center and relying on the retinal feedback. This is an abnormal and relatively ineffective method of control, somewhat analogous to the control of the legs by visual guidance in tabes dorsalis. If, however, a real adjustment is made with partial success, so that a new relationship obtains between the impulses sent from the conjugate innervation center to the space-

representation region and the amount of retinal feedback to be expected, then the environment may cease moving. Analogous reasoning will explain why motion of the environment stops after nystagmus has persisted for a relatively long time.

Finally, let us consider the interesting experiment reported by Adler,[17] which he described as follows[18]:

> A patient with a paresis of a right lateral rectus muscle was seated at a Zeiss perimeter, and the left eye was covered. A test spot of light was then placed on the arc of the perimeter in the temporal field 30 degrees from fixation. A black cloth was held in such a way that the patient could not see his own arm, and he was asked to point directly to the test spot of light. The difference between the actual position of the spot and the position to which he pointed was then measured: Two types of test objects were used interchangeably: (1) A large white spot of light, measuring 15 mm. in diameter, and (2) a small spot of light, measuring 2 mm. in diameter, illuminating a letter which had to be identified by the subject. The letter was small enough that the subject had to move the eyes so that its image fell on the fovea before he could identify it. In each trial the letter was changed. It was found that when the large spot of light was used, i. e., target 1, the angle of past-pointing was much larger than when the small spot and letter target 2 was used.

In this situation the fixation reflex occurs automatically but inadequately. When the large test object is used, the task presented to the subject is such that he can obtain what is to him a satisfactory performance, even though the test object is not imaged on the fovea. In this situation the inadequacy of the fixation reflex is not compensated, and past pointing occurs. When, however, the small test object is used, the subject cannot perform the task he is given, namely, to read the letter, unless the image is made to fall on the fovea. This the patient accomplishes by forcing his eye farther over by strong voluntary innervation through relying on his acquired learned relationship between the amount of conjugate innervation sent out and the amount of retinal displacement to be expected. Thus, by substituting voluntary innervation for the deficiency of innervation arising from the fixation reflex, he achieves fixation and reduces or substantially eliminates the amount of past-pointing error.

SUMMARY AND CONCLUSIONS

The hypothesis here presented is that, in the absence of articular sensitivity and with exteroceptive feedback from the retina ineffective for the provision of an error signal, the ocular movements of fixation and pursuit are controlled to a substantial extent by parametric feedback from the extraocular muscles. The hypothesis is applied in the qualitative explanation of various normal and abnormal ocular movements and the accompanying perception of movement, or lack thereof, of the eyes and the environment.

17. Adler, F. H.: Pathologic Physiology of Convergent Strabismus: Motor Aspects of Non-accommodational Type, Arch. Ophth. **33**:362, 1945.

18. Adler, F. H.: Physiology of the Eye: Clinical Application, St. Louis, C. V. Mosby Company, 1950, p. 339.

SYPHILITIC OPTIC NERVE ATROPHY TREATED WITH PENICILLIN

Observations Two to Six years After Treatment

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ATLANTA

PENICILLIN has been employed in the treatment of syphilis for a number of years, but there is still little information as to its efficacy in the treatment of primary optic nerve atrophy caused by this infection. Although fever therapy is known to be of considerable value in this condition, it is often associated with severe untoward reactions, especially in aged or infirm patients. The arsenicals and heavy metals are not very effective agents in the treatment of optic nerve atrophy, and it is important to assess the value of penicillin in this condition.

In this paper, data are presented in regard to the use of penicillin in the treatment of progressive primary atrophy of the optic nerve due to syphilis.

There are relatively few reports on the treatment of syphilitic optic nerve atrophy with penicillin alone or in combination with fever. The largest number of cases has been reported by Klauder,[1] who in 1948 described his results in 49 patients. He increased this total to 56 patients in 1949, and to 80 patients in 1951.[2] In these studies, patients treated with penicillin alone and those given combined penicillin and fever therapy have been considered together, and it is difficult, therefore, to evaluate the effect of penicillin alone. Fifty of the 80 patients had stationary vision and arrest of the disease one to six years after therapy.

In 1948, Lamotte [3] reported satisfactory response in two-thirds of 31 patients with optic nerve atrophy treated with penicillin. In this report no information was given as to the dose of penicillin, and at that time approximately one-third of the

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This study was aided by a grant from the United States Public Health Service.

Read at a Symposium of the American Venereal Disease Association on "Recent Advances in the Treatment of Venereal Diseases," Washington, D. C., May 1, 1952.

From the Department of Ophthalmology, Emory University School of Medicine, and Clay Memorial Eye Clinic, Grady Memorial Hospital (Dr. Benton), and the Georgia Department of Public Health and the Clinic of Genito-Infectious Diseases, Grady Memorial Hospital, Emory University School of Medicine (Dr. Harris).

1. Klauder, J. V.: Penicillin in the Treatment of Primary Optic Atrophy, Recent Adv. Study Ven. Dis., pp. 233-236, 1948.

2. Klauder, J. V., and Gross, B. A.: Penicillin Treatment of Syphilitic Primary Optic Atrophy, Am. J. Syph. **33**:234-242, 1949. Klauder, J. V., and Meyer, G. P.: Early Diagnosis of Syphilitic Primary Optic Nerve Atrophy, Arch. Ophth. **43**:537-552, 1950. Klauder, J. V.: Blindness Due to Syphilis, J. Ven. Dis. Inform. **32**:183-192, 1951.

3. Lamotte, W. O., Jr.: Sixty Cases of Primary Optic Atrophy Critically Studied from the Standpoint of Diagnosis and Therapy, Recent Adv. Study Ven. Dis., pp. 238-245, 1948.

patients had been followed for less than two years. Horne and Curtis [4] reported results in four patients with syphilitic optic nerve atrophy treated with penicillin. All had slight to moderate visual impairment and retained "useful" vision for the more than one year of observation.

MATERIAL

The material for the present study consists of 23 patients with progressive syphilitic primary atrophy of the optic nerve. A summary of the entire group of patients is presented in Table 1. All the patients were Negroes. Only one (Patient 1) had evidence of congenital syphilis. Manifestations of tabes dorsalis were present in five (Patients 10, 16, 17, 20, and 22); one (Patient 7) had hemiplegia caused by meningovascular syphilis. The spinal fluid in every case showed an increased number of cells, increased protein, and a strongly positive Wassermann reaction.

TABLE 1.—*Summary of Data on Twenty-Three Patients with Syphilitic Primary Atrophy of the Optic Nerve Treated with Penicillin*

			Visual Acuity Before Treatment				Final Visual Acuity		
Patient	Age	Sex	Right Eye	Left Eye	Units of Penicillin (Millions)	Follow-Up (Mo.)	Right Eye	Left Eye	Final Visual Status
1	12	M	20/20	20/20	4.8	39	20/30	20/30	Stationary
2	49	M	20/25	20/25	4.8	43	20/25	20/25	Stationary
3	50	M	20/30	L. P.	5.4	67	20/40	H. M.	Stationary
4	61	F	20/30	Blind	6.0	56	20/40	Blind	Stationary
5	61	M	H. M.	20/40	4.8	20	H. M.	20/40	Stationary
6	67	M	20/50	20/200	4.8	40	20/70	20/200	Stationary
7	47	M	8/200	20/50	6.0	63	8/200	20/70	Stationary
8	41	M	20/70	20/100	6.0	73	6/200	4/200	Progressive loss
9	58	M	20/100	20/100	18.0	40	Blind	L. P.	Progressive loss
10	47	F	L. P.	20/70	5.83	57	Blind	20/60	Stationary
11	55	M	20/70	C. F.	12.0	40	20/100	C. F.	Stationary
12	58	M	20/400	20/100	2.4	68	L. P.	5/200	Progressive loss
13	44	F	C. F.	20/200	6.0	24	H. M.	8/200	Progressive loss
14	69	M	20/200	Blind	6.0	30	Blind	Blind	Progressive loss
15	68	M	10/200	C. F.	4.8	43	20/200	H. M.	Stationary
16	50	M	C. F.	C. F.	6.8	66	H. M.	L. P.	Progressive loss
17	56	M	C. F.	C. F.	8.4	32	Blind	Blind	Progressive loss
18	49	M	C. F.	L. P.	9.0	31	H. M.	Blind	Progressive loss
19	70	M	H. M.	H. M.	8.4	35	L. P.	L. P.	Progressive loss
20	53	F	H. M.	H. M.	8.4	36	Blind	L. P.	Progressive loss
21	56	M	L. P.	C. F.	6.0	48	Blind	H. M.	Progressive loss
22	56	F	L. P.	L. P.	4.8	53	L. P.	Blind	Progressive loss
23	43	M	H. M.	Blind	6.0	64	L. P.	Blind	Progressive loss

The diagnosis of optic nerve atrophy was made on the basis of decreased visual acuity (not improved with lenses), pallor of the optic disks, and visual field defects, usually manifested by an asymmetrical peripheral contraction.

Visual acuity before treatment ranged from 20/20 to nearly complete blindness. Seven patients had vision better than 20/70 in one or both eyes; seven others had visual acuity between 20/70 and 20/200, and the remaining nine had vision worse than 20/200 in the better eye. The visual acuity was normal, or nearly normal, in two patients (1 and 2), and the diagnosis for these patients was made on the basis of pallor of the optic disks and defects in the visual fields. The history of recent visual disturbances and the slight decrease in visual acuity and size of visual fields observed during the treatment period were considered evidences of the progressive nature of the condition in these two patients. The visual-field measurements were made on a standard perimeter with a 5-mm. white test object (5/330 form). The peripheral field defects in the patients who could be satisfactorily tested (Patients 1 through 15) are illustrated in Figures 1 and 2. Tangent-screen perimetry was not done routinely. All but three patients were treated

4. Horne, S. F., and Curtis, A. C.: The Treatment of Primary Optic Atrophy with Penicillin and with Penicillin and Malaria, Am. J. Syph. **33**:143-151, 1949.

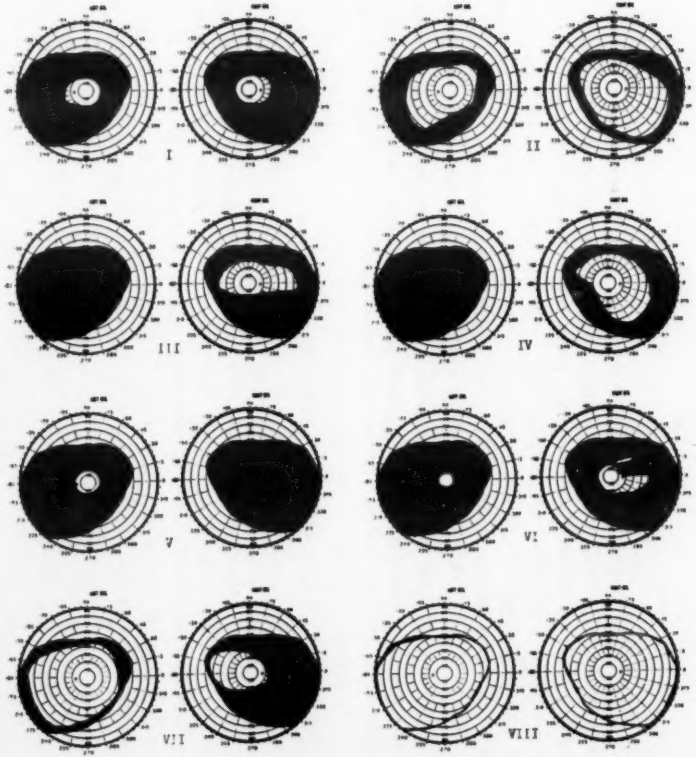

Fig. 1.—Initial visual fields (Cases 1-8).

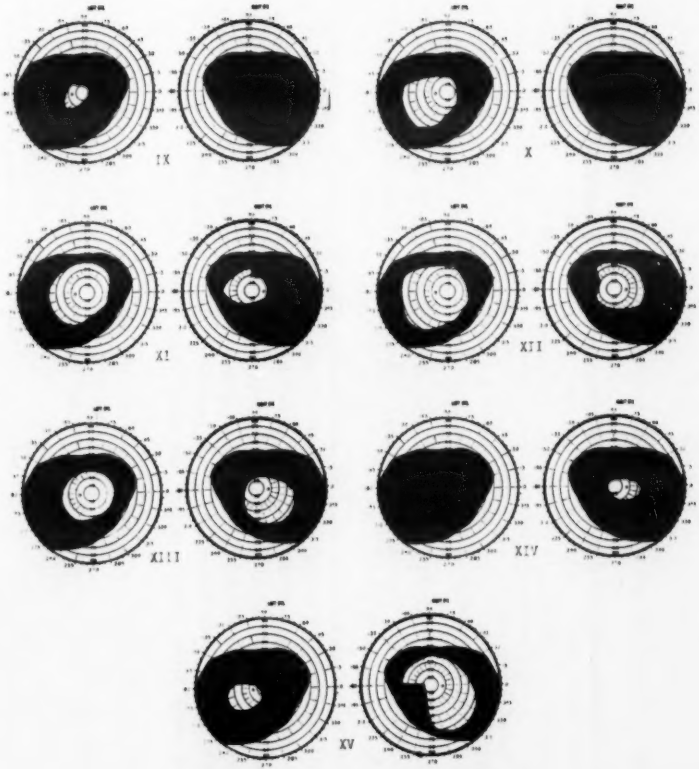

Fig. 2.—Initial visual fields (Cases 9-15).

with crystalline penicillin G in aqueous solution in doses ranging from 2,400,000 to 8,400,000 units. These three patients (9, 11, and 18) received 18,000,000, 12,000,000, and 9,000,000 units, respectively, of penicillin in oil and wax. Two patients (12 and 23) were given a second course of penicillin because of continued loss of vision following their initial treatment. The entire group of patients has been observed over a period of 20 to 73 months, with an average follow-up period of 48 months.

RESULTS

The visual acuity in 10 of the 23 patients was unchanged 20 to 67 months after treatment. The remaining 13 patients had progressive visual impairment. All seven patients with pretreatment visual acuity of 20/50 or better in one or both eyes retained the same vision 20 to 67 months after treatment. Seven other patients, with moderately impaired vision in one or both eyes (20/70 to 20/200), showed a less satisfactory response; the vision of two has remained stationary for four years, and in five visual impairment has progressed beyond the stage of useful vision, with one becoming completely blind. Nine patients were industrially blind (vision less than 20/200 in the better eye) before treatment. Eight in this group continued to lose visual acuity after treatment, one being blind 32 months later.

TABLE 2.—*Classification of Patients on Basis of Visual Acuity Before Treatment and Results of Treatment*

Before Treatment		Visual Results of Treatment	
Visual Acuity (Better Eye)	No. of Patients	Stationary	Progressive Loss
20/20-20/50	7	7	0
20/70-20/200	7	2	5
Worse than 20/200	9	1	8
	23	10	13

The correlation observed between the degree of visual impairment before treatment and the outcome of therapy is shown in Table 2 and Figure 3. Two patients (12 and 23) were re-treated because their vision became worse after the first course of penicillin. The patient who received only 2,400,000 units of penicillin was given an additional 6,000,000 units 17 months later; no further diminution of vision has occurred during the past 4 years. The other patient continued to lose vision despite an additional 9,600,000 units of penicillin, given seven months after the first course.

The spinal fluid cell count became normal in all patients and has remained normal even when optic nerve atrophy progressed. The spinal fluid protein also became normal in all but one patient (Patient 8), whose vision continued to grow worse. The Wassermann reaction of the spinal fluid became normal in four patients, all of whom retained the same vision after treatment.

COMMENT

These results indicate that penicillin is effective in arresting the early stages of optic nerve atrophy caused by syphilis. All patients with vision of 20/50 or better obtained a satisfactory result with treatment, whereas patients with vision worse than 20/50 usually had further visual loss. This critical level of pretreatment vision is apparently of prognostic significance and corresponds closely to the figure of

20/60 given by Moore [5] as an important factor in predicting the outcome of malaria therapy.

A comparison of the present and the previous status of patients reported by one of us (C. D. B.)[6] in 1948 reveals that all the patients considered as showing arrest of optic nerve atrophy at that time have retained the same vision for the subsequent 3½ years. It is interesting in this connection that when diminution of vision progressed it usually did so within 1½ years.

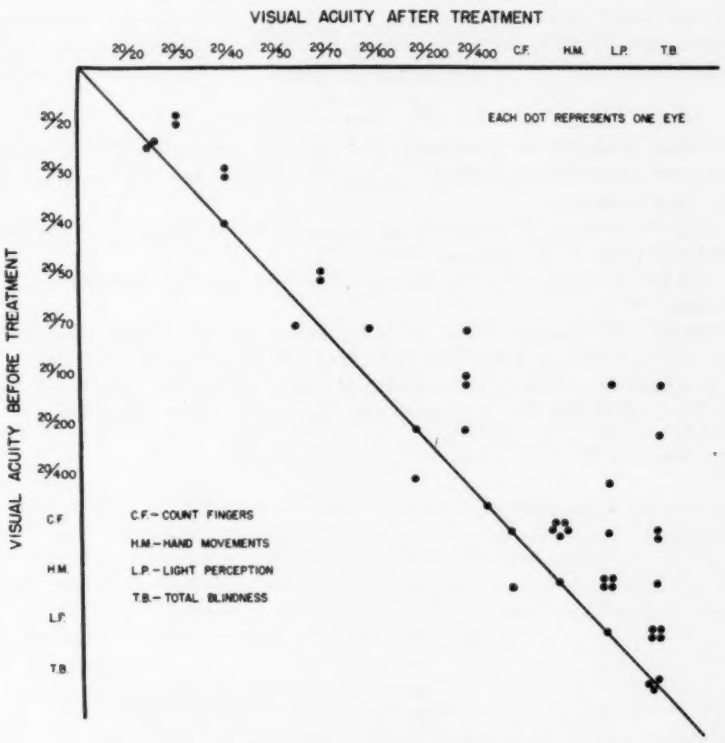

Fig. 3.—Comparison of visual acuities before and after penicillin treatment for 23 patients with syphilitic optic nerve atrophy.

Five of the seven patients with pretreatment vision of 20/70 to 20/200 became industrially blind. These patients had a history of rather rapid loss of vision, and penicillin treatment did not seem to influence this downhill course. The other two patients (11 and 12), whose vision remained unchanged after treatment, had a history of slower loss of vision.

5. Moore, J. E.; Kemp, J. E., and others: The Modern Treatment of Syphilis, Ed. 2, Springfield, Ill., Charles C Thomas, Publisher, 1943.

6. Benton, C. D., Jr., and Heyman, A.: Treatment of Ocular Syphilis with Penicillin, Arch. Ophth. **40**:302-310, 1948.

The dose of penicillin found to be effective in the treatment of early optic nerve atrophy ranged from 4,800,000 to 6,000,000 units. This amount of penicillin failed to prevent further visual loss in patients with visual acuity worse than 20/50. Whether the loss of vision in these patients could have been prevented by larger doses of penicillin is not known, but we believe that it is probably wise to employ much larger doses than were used in this study when treating such patients, especially if their vision is failing rapidly.

Results of penicillin treatment roughly parallel those of malaria therapy. Fever treatment usually fails to prevent further visual loss in patients whose visual acuity is worse than 20/50; it also is sometimes dangerous to the patient. In spite of this, it might be advisable to combine fever with penicillin in treating some such patients.

SUMMARY AND CONCLUSIONS

Twenty-three patients with progressive syphilitic primary atrophy of the optic nerve were treated with one course of penicillin and observed for an average of four years after therapy.

Satisfactory arrest of visual loss was obtained in the seven patients whose initial visual acuity was 20/50 or better.

The dose of penicillin found to be effective in these cases was 4,800,000 to 6,000,000 units.

All but 3 of 16 patients whose vision was worse than 20/50 failed to retain their same vision, despite treatment with 6,000,000 to 18,000,000 units of penicillin.

Information is needed as to whether larger doses of penicillin alone or combined with fever will be beneficial to patients with moderate or severe visual damage.

REGRESSION OF METASTATIC LESIONS OF BREAST CARCINOMA FOLLOWING STERILIZATION

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THE PURPOSE of this paper is to report two cases of metastatic lesions from breast carcinoma which showed marked regression following sterilization by x-rays. Typical metastatic lesions in the choroid of both eyes in one case and lung metastases in both cases showed decided improvement after sterilization.

The prognosis for patients with carcinoma of the breast in whom metastases to distant structures, such as the lung or eye, have developed is considered hopeless. Radical excision of the primary tumor with or without local x-ray therapy may be indicated. This usually has no effect upon the metastases. Recent developments in therapy, however, have shown some promise in retarding the course of the disease. Among these measures for treating metastatic breast carcinoma are the use of hormones and castration. While the modes of action are unknown, it has been noted that alteration of the hormonal status of the patient by sterilization or hormonal therapy may profoundly influence the course and the character of advanced breast carcinoma.[1]

The survival rate for castrated patients after the appearance of the metastases was found by Thayssen [2] to be 40% for two years or more, while the corresponding figure for the controls was only 11% (Fig. 1). After five years, 20% of the castrated patients are still alive, while all the patients of the control group have died.

The principles of treatment of advanced breast carcinoma with hormonal therapy and sterilization [3] are presented in the following outline:

I. Castration
   (*a*) Results: Remission in 20 to 40% of cases
   (*b*) Duration: Variable; may be more than five years
   (*c*) Age: More in young women (may be effective 10 years beyond menopause)
   (*d*) Untoward effect: Menopausal symptoms (control with testosterone; never estrogen)

Read before the College of Physicians of Philadelphia, Section on Ophthalmology, Feb. 21, 1952.

From the Department of Ophthalmology, Hospital of the University of Pennsylvania, the University of Pennsylvania School of Medicine, and the Children's Hospital.

1. Nathanson, I. T.: Sex Hormones and Castration in Advanced Breast Cancer, Radiology **56**:535 (April) 1951.

2. Thayssen, V. E.: Influence of Castration by Roentgen on Carcinoma of the Breast, Acta radiol. **29**:189, 1948.

3. Current Status of Hormone Therapy of Advanced Mammary Cancer, Report of the Committee on Research of the Council on Pharmacy and Chemistry, J. A. M. A. **146**:471 (June 2) 1951.

II. Androgen (testosterone): 285 cases

(*a*) Results:
Subjective: Pain, anorexia, etc., 62%
Objective: Bone and soft tissue, 20%

(*b*) Duration: More than 9 months in 20%

(*c*) Age: Effective at any age

(*d*) Dose: 50 mg. three times a week, intramuscularly; persist at least 3 months

(*e*) Untoward effects:
Masculinization
Salt retention
Edema
Cardiac failure
Hypercalcemia

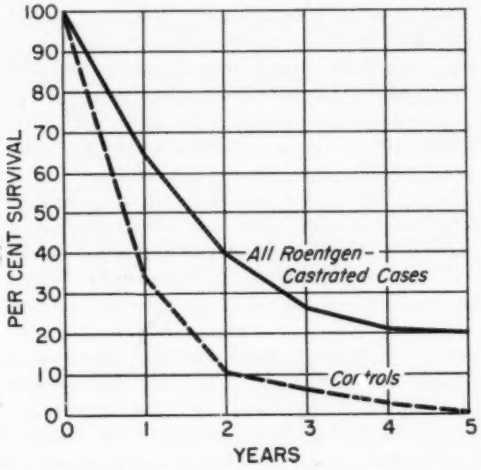

Fig. 1.—The five-year survival of castrated and noncastrated patients, reckoned from the appearance of metastases (after Thayssen [2]).

III. Estrogen (diethylstilbestrol): 144 cases

(*a*) Results:
Subjective: Pain, anorexia, etc., 60%
Objective: Regression bones and soft tissue, 50%

(*b*) Duration: 9 months in 50%

(*c*) Age: 60 years or more; may accelerate tumor growth in young women

(*d*) Dose: 15 mg. a day; persist more than 5 months

(*e*) Untoward effects:
Bleeding (withdrawal)
Salt retention
Edema
Cardiac failure
Hypercalcemia

Histologic examination of biopsy and autopsy material collected in this study has not revealed any change in tumor cells or stroma which suggests an explanation of the mechanism of hormonal action in metastatic breast carcinoma.

REPORT OF CASES

CASE 1.—H. S., a nurse aged 31, was first seen by one of us (H. G. S.) on Aug. 22, 1949, because of blurred vision in the left eye of one month's duration. The past medical history revealed that on Aug. 7, 1947 she had a radical mastectomy for adenocarcinoma of the breast. Since the operation, the patient had felt fine, had had no evidence of recurrence, and had gained 20 lb. (9.1 kg.). Vision was 6/6 in the right eye and was corrected to 6/15 in the left. Ophthalmoscopic examination revealed a normal right eye. However, the left fundus presented a typical metastatic lesion with 4 D. of elevation at one point. Transillumination revealed a normal condition, and intraocular tension was normal. The visual fields showed a large central defect corresponding to the lesion in the fundus. In view of the past history and the fundus lesion, a diagnosis of metastasis to the eye from breast carcinoma was made, and the patient was admitted to the Hospital of the University of Pennsylvania. Physical examination showed an entirely normal status except for the mastectomy scar. A thorough survey revealed a number of small dense nodules, probably representing metastases, in the chest. After consultation with two other ophthalmologists, it was concluded that the kindest course was to enucleate the left eye, telling the patient that the lesion very possibly was an isolated one.

On Aug. 26 the left eye was enucleated. Pathologic examination of the globe revealed metastasis to the choroid from carcinoma of the breast. There was a moderate degree of invasion of the choroid. The appearance of the tumor was similar to that of the breast carcinoma obtained from the same patient.

The patient was told that, for reasons of precaution, sterilization should be performed. A sterilizing dose of radiation to the ovaries was therefore started on Sept. 2, 1949. After this procedure, the densities in the lung entirely disappeared.

The patient felt well aside from some menopausal symptoms, which were controlled with phenobarbital, until May, 1951, when she began to experience chest pain. In September, 1951, x-ray examination revealed large metastatic lesions in both lung fields and a pleural effusion on the left. At this time a vaginal smear showed a definite increase in estrogen activity, and another sterilizing dose of x-rays was given.

However, the second course of radiation did not alter the progress of the disease. In February, 1952, testosterone therapy was started, and the patient is now receiving this therapy. The last ophthalmologic examination, in March, 1952, showed that the right eye has remained normal.

CASE 2.—H. Y., a white woman aged 40, had a radical mastectomy for breast carcinoma in September, 1949, and local irradiation in March, 1950. She first consulted one of us (H. G. S.) 10 months later, on July 17, 1950, because of blurring of vision in the right eye for the past three months. Visual acuity with best correction was 6/15 in each eye. The ophthalmoscopic examination of the right eye showed a pale, pigmented lesion with 8 D. of elevation. The left eye had two similar lesions, slightly less elevated. The intraocular tension was normal. There were large central scotomas corresponding to the fundus lesions in the visual fields. The diagnosis of metastasis to the choroid of both eyes was made, and the patient was admitted to the Hospital of the University of Pennsylvania. The patient complained of anorexia, a nonproductive cough, and back pain. Complete physical examination revealed nothing abnormal except for several recurrent subcutaneous nodules in and around the mastectomy scar. X-ray studies showed metastatic carcinoma involving the lungs, skull, cervical portion of the spine, ribs, pelvis, and femurs.

Ovarian castration by means of x-ray therapy was performed from July 18 to Aug. 4, 1950. One month later the patient had gained weight and felt rather well; the back pains had subsided, and her vision had improved. Examination two months later revealed that the skin nodules had disappeared. There was also regression of the metastatic lesions in the lungs (Figs. 2 and 3) and bones, and the ocular lesions had cleared entirely, leaving scattered areas of retinal atrophy. The ocular lesions, previously elevated 8 D., were then at the same level

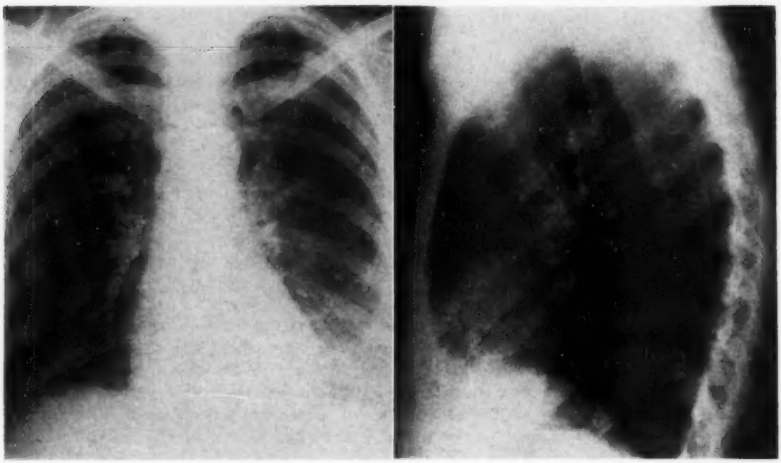

Fig. 2 (Case 2).—Roentgenograms of chest before sterilization (July 17, 1950), the appearance being typical of metastatic carcinoma.

Fig. 3 (Case 2).—Roentgenograms of chest after sterilization (Oct. 4, 1950), showing definite evidence of improvement.

as the disk. The site of the tumor appeared atrophic, pigmented, and much more like an old pigmented choroiditis than neoplasm. The visual acuity was equal to counting fingers in the right eye and was 6/6—4 in the left eye. However, in about three months the patient suffered a relapse and died eight months later, despite treatment with testosterone.

SUMMARY

Two cases of carcinoma of the breast accompanied by metastatic lesions are reported. In both cases lung metastases cleared, and in one case metastatic lesions in the choroid disappeared remarkably after sterilization by x-radiation. To the best of our knowledge, the latter observation has not been recorded previously.

A SIMPLIFIED BLASKOVICS OPERATION FOR BLEPHAROPTOSIS

Results in Ninety-One Operations

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THE CONSENSUS of ophthalmologists seems to be that resection of the levator is the operation of choice for all cases of blepharoptosis in which the levator muscle is active. Of the 26 operations [1] designed to shorten this muscle, the Blaskovics operation seems to be the most popular. Surgeons who prefer to utilize the superior rectus or the frontalis muscle for all types of ptosis as a primary procedure do so because the Blaskovics procedure seems complicated or because no one seems to know just how much levator tissue to excise in each case.

The purpose of this article is to present a simplified procedure for shortening the levator palpebrae muscle, to demonstrate what types of ptosis are most suitable for this procedure, and to suggest a simple rule for determining how much levator tissue should be excised in a given case.

BLASKOVICS OPERATION FOR RESECTION OF THE LEVATOR PALPEBRAE MUSCLE

In 1929 Blaskovics [2] described his latest method for shortening the levator as follows [2b]:

> The upper lid is everted by means of a lid-holder, and the operative field is anesthetized by an injection of 2 cc. of a procaine hydrochloride and epinephrine solution under the conjunctiva of the fornix. In the conjunctiva, thus stretched, one can easily make an incision along the convex border of the tarsus with a scalpel without cutting the underlying levator. If the incision is not made too near the tarsus, the wound gapes at once, and one can proceed immediately to introduce the three interrupted sutures into the proximal edge of the incision in the conjunctiva. This is done in such a manner that the loops of the suture lie on the epithelial side of the conjunctiva. One now grasps the three sutures at once and pulls on them; while traction is thus exerted, the conjunctiva is easily separated from the muscle with a pair of scissors. This separation should be continued upward for quite a distance.
>
> After completely exposing the levator one inserts in this muscle three fixation sutures. A firm bundle of the levator is seized with toothed forceps and a strong thread is passed through it and tied. The three sutures introduced are also tied. By pulling on the fixation sutures, the levator can be incised easily with scissors without injuring the fascia praetarsalis, and the levator distal to the fixation sutures is completely divided. The muscle should be freed on both sides so that it can be pulled forward readily with the fixation sutures.

From the Institute of Ophthalmology, Columbia-Presbyterian Medical Center.

Read at the Eighty-Seventh Annual Meeting of the American Ophthalmological Society, White Sulphur Springs, W. Va., June 7-9, 1952.

1. Berke, R. N.: Blepharoptosis, Arch. Ophth. **34**:434-450 (Nov.-Dec.) 1945.

2. de Blaskovics, L.: (*a*) A New Operation for Ptosis with Shortening of the Levator and Tarsus, Arch. Ophth. **52**:563-573 (Nov.) 1923; (*b*) Treatment of Ptosis: Formation of a Fold in the Eyelid and Resection of the Levator and Tarsus, Arch. Ophth. **1**:672-680 (June) 1929.

With this traction the anterior surface of the levator can also be freed, but care must be taken not to injure the fascia. The fibers of the muscle passing to the skin should also be divided. The muscle can then be drawn free out of the orbit. With the aid of fixation sutures, it is now easy to pass the conjunctival sutures from behind forward at the correct height through the muscle. While pulling on the sutures, one divides the levator completely distal to the sutures introduced. A piece of the muscle is thus resected together with the fixation sutures.

The eyelid now falls back to its normal position and the lid-holder is applied in the usual manner. One seizes the connective tissue-muscle sutures with a forceps, pulls the muscle forward and then introduces into the levator the sutures which produce the folding of the eyelid. These are introduced into the muscle in the same manner as the fixation sutures. They should not be placed too high in the muscle. Normally, the attachment of the levator to the skin occurs at about the level of the convex edge of the tarsus. The tarsus should be reduced, however, to about half of its normal size. The new point of attachment should be from 4 to 5 mm. above this, so that the fold-producing sutures in the eyelid are introduced from 4 to 5 mm. above the line of incision of the muscle.

Before these can be passed through the skin, one must remove a portion of the tarsus. In order to do this one everts the lid again, seizes the stump of the muscle on the convex edge of the tarsus with a pair of forked forceps and pulls the everted lid over a lid plate inserted from below. In about its center the tarsus is now divided longitudinally and removed with a pair of scissors. If it seems necessary to remove more, the tarsus can be reduced to even 1.5 mm. A narrow strip of tarsus bends, owing to the increased upward pull of the levator, and thereby widens the palpebral fissure a great deal more than the stretching of the muscle alone could have done.

After removing a sufficiently large portion of the tarsus, one replaces the lid in its normal position and completes the fold-forming sutures. The interrupted sutures introduced into the muscle are passed through the lid from behind forward at the height at which one wishes to have the fold of the eyelid. At this point one usually sees fine wrinkles passing along the lid so that the level at which the sutures should be inserted can be easily determined. Even before one ties the sutures, one sees the fold appear in the eyelid. After they are tied, not too tightly, the knots disappear in the depths of the newly formed fold. One does not cut off the ends of the sutures but proceeds at once to the last step of the operation, fixation of the stump of the levator.

The conjunctiva-muscle sutures still hang out of the palpebral fissure. First, the forceps on them is taken off. It is unnecessary to suture the muscle to the stump of the tarsus. The muscle unites with it just as well when the sutures are pulled close over the edge of the incised tarsus through the eyelid. This is likewise performed from behind forward; in doing this one should take care that the sutures are brought through the skin neither too high nor too low. In the first case the skin of the lid would be pushed toward the edge of the lid and as a result the eyelashes would come to be directed downward; in the second case, ectropion would in all probability develop. Both errors in technique can easily be avoided if one does not displace the skin of the eyelid in pushing the needle through it but instead pushes it directly through the part of the skin raised by the point of the needle.

After these sutures are tied, their ends are cut off. The sutures forming the fold in the lid, however, are preserved and are used to assure closure of the eye under the bandage. For this purpose one attaches them, at the correct tension, to the cheek by means of adhesive plaster. The attachment of the ends of these sutures can be increased with a second strip of adhesive after bending them backward. After twenty-four hours these sutures can be divided in the usual manner, and the adhesive plaster can be removed. From now on the eye is protected by a Fuchs shield. On the sixth day all the sutures are removed. The levator always heals smooth with the stump of the tarsus, although it was brought only close to it. The point of exit of the fold-forming sutures becomes the highest point of the skin fold.

This procedure is unnecessarily complicated and is likely to lead the inexperienced surgeon into several pitfalls.

1. Incision of the conjunctiva at the upper edge of the tarsus makes reflection of the conjunctiva from Mueller's muscle tedious because of the troublesome bleed-

ing which always occurs. It also predisposes to buttonholing of the conjunctiva and to reflection of Mueller's muscle with the conjunctiva.

2. In passing the three traction sutures through Mueller's muscle and the aponeurosis, one may accidentally pick up the septum orbitale. Should this occur, the septum orbitale may be resected with the levator muscle.

3. Blaskovics correctly emphasized that it is necessary in some cases to remove as much as 20 mm. of relaxed levator tissue in order to procure adequate correction, but he failed to state that in order to accomplish this it is necessary to free the levator from its attachments to the lateral orbital tubercle, laterally, and to the pulley of the superior oblique muscle, medially. If these attachments are not freed, notching of the upper lid nasally or inadequate correction may occur.

It is unnecessary to place six sutures (two sets of three sutures each) in the levator muscle in order to anchor the levator to the upper lid and produce a natural-appearing upper lid fold, because one set of sutures properly placed and tied suffices for both purposes.

5. It is undesirable to excise all except 1.5 mm. of the tarsus along the lid margin, as advocated by Blaskovics, because this procedure weakens the body of the upper lid so that it becomes flimsy, with a tendency to ectropion or entropion. If the levator muscle is adequately freed from its attachments to the lateral orbital tubercle and to the pulley of the superior oblique muscle, sufficient resection of the levator is possible without a large tarsectomy.

6. Pulling the upper lid down to cover the cornea postoperatively should be avoided because this maneuver places extra tension on the sutures, thus increasing the danger of pulling them out of the levator. Furthermore, it is impossible to pull the lid down sufficiently to cover the cornea in some cases because of the nonelasticity of the levator tissues. A better and safer protection to the cornea is to pull the lower lid up by means of two modified Frost sutures.[3]

7. Failure to place a firm pressure dressing over the eye for the first four or five postoperative days predisposes to intense edema of the upper lid and to pulling out of the sutures.

ANATOMY OF UPPER LID

A thorough knowledge of the anatomical layers of the upper lid is necessary to perform resection of the levator satisfactorily. Therefore a brief review of the anatomy will be given here.

Layers of Tissue in the Upper Lid.—The lower part of the upper lid is composed of four surgical layers of tissue: skin, orbicularis, pretarsal tissues, and tarsus (Figs. 1 and 2).[4] The upper part of the lid, however, is made up of seven layers: (1) skin, (2) orbicularis muscle, (3) septum orbitale, (4) roll of orbital fat, (5) levator aponeurosis, (6) Mueller's muscle, and (7) conjunctiva. It should be noted that Mueller's muscle ends in the upper edge of the tarsus, but the levator aponeuro-

3. Frost, A. D.: Supporting Suture in Ptosis Operations, Am. J. Ophth. **17**:633 (July) 1934.

4. The conjunctiva is so firmly fused to the tarsus that the two structures cannot be separated surgically. The pretarsal tissues, made up of the posterior fascial lining of the orbicularis muscle and the terminal fibers of the levator aponeurosis, are usually reflected surgically with the orbicularis muscle. Therefore, the pretarsal tissue layer is seldom identified as a distinct surgical layer in operations on the upper lid.

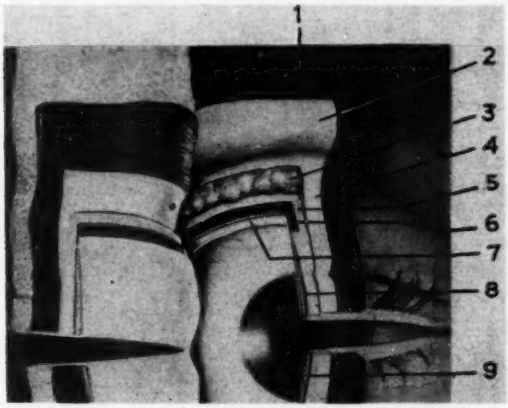

Fig. 1.—Anatomy of lids, frontal view. The tissues of the lids and brow have been incised in the vertical plane and turned laterally. *1*, orbicularis muscle; *2*, periosteum of frontal bone; *3*, orbital fat; *4*, septum orbitale; *5*, levator aponeurosis; *6*, Mueller's muscle; *7*, conjunctiva; *8*, upper tarsus; *9*, lower tarsus. Note that Mueller's muscle inserts into the upper edge of the tarsus but that the aponeurosis ends in the tissues anterior to the tarsus, producing the upper lid fold.

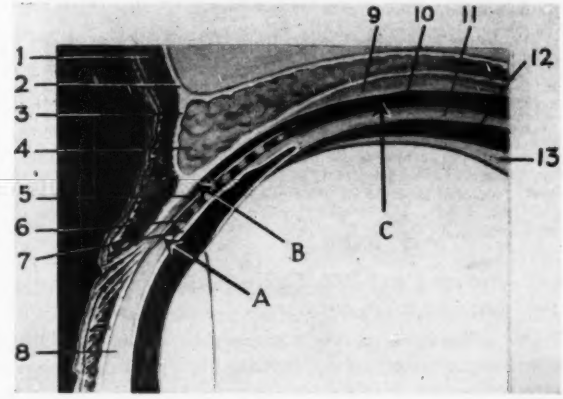

Fig. 2.—Sagittal section of upper lid and levator muscle. *1*, orbicularis muscle; *2*, periosteum of frontal bone; *3*, septum orbitale; *4*, orbital fat; *5*, levator aponeurosis; *6*, Mueller's muscle; *7*, conjunctiva; *8*, tarsus; *9*, sheath and check ligament of levator; *10*, skeletal muscle fibers of levator; *11*, conjoined sheath and Tenon's capsule; *12*, superior rectus muscle; *13*, Tenon's capsule. Note that the septum orbitale joins the levator aponeurosis at *B* in this specimen, that the aponeurosis divides into numerous fibrillae below the upper border of the tarsus, and that Mueller's muscle ends in the upper border of the tarsus. *A-C* represents the amount of levator tissue to be excised in the average case of congenital ptosis.

sis extends forward beyond this point 2 to 3 mm. to become fused with the anterior surface of the tarsus, the orbicularis muscle, and the skin. The last connection produces the upper lid fold and supports the skin and the lashes from falling down over the cornea. The septum orbitale fuses with the aponeurosis somewhere between *A* and *B* in Figure 2, and from this point the two structures pass downward anterior to the tarsus as one fused membrane. This close approximation of the septum orbitale to the aponeurosis (*A* to *B*, Fig. 2) must be kept in mind in freeing the levator, because the septum orbitale may be inadvertently picked up with the aponeurosis and the two structures dissected upward together. Should this occur, the plane of dissection will be anterior to the septum orbitale rather than posterior to it. The anterior, or upper, plane of dissection should be between the septum orbitale and the aponeurosis, and not between the septum orbitale and the skin. The posterior, or lower, plane of dissection should be between Mueller's muscle and the conjunctiva.

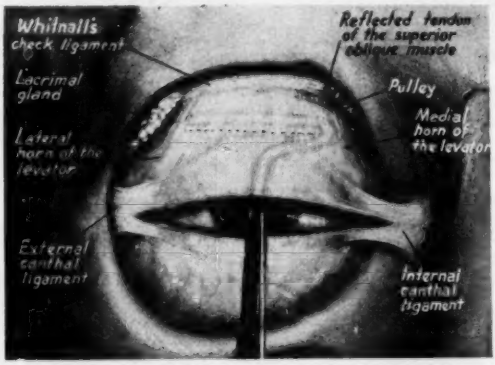

Fig. 3.—Insertions of the levator aponeurosis. Phantom view of the position of the ptosis clamp preparatory to freeing the aponeurosis in resection of the levator muscle. Note the close relationship between the medial third of Whitnall's check ligament and the reflected tendon of the superior oblique muscle. The dotted line indicates the site of incision in severing the aponeurosis from the tarsus.

The distance between *A* and *C* in Figure 2 represents the amount of levator tissue which should be removed in the average case of congenital ptosis.

Whitnall's Check Ligament of the Levator.—In 1911 Whitnall [5] described a band of condensed areolar tissue extending from the pulley of the superior oblique muscle across the upper surface of the levator to the lacrimal gland (Fig. 3). This band acts normally as a check ligament for the levator muscle to prevent its overaction. It also restricts pulling of the muscle forward when one is resecting the levator.

The lateral extremity of Whitnall's ligament passes into the substance of the lacrimal gland. This part of the ligament is so elastic that it is never necessary to incise it in freeing the levator muscle in ptosis operations.

5. Whitnall, S. E.: On a Ligament Acting as a Check to the Action of the Levator Palpebrae Superioris Muscle, J. Anat. & Physiol. **45**:131, 1911; Anatomy of the Human Orbit and Accessory Organs of Vision, Ed. 2, Oxford University Press, 1932.

Medial and Lateral Horns of the Levator Muscle.—The levator aponeurosis fans out as it passes forward and downward (Fig. 3), the central portion becoming attached to the tissues anterior to the tarsus (Fig. 2). The lateral part of this tendon (known as the lateral horn) becomes inserted into the external canthal ligament and the lateral orbital tubercle. The medial part (known as the medial horn) becomes attached to the internal canthal ligament and the posterior lacrimal crest.

The lateral horn is thicker and more fibrous than the medial. Because the latter is thin and flimsy, and because it is freed when the check ligament is incised, it is rarely necessary to identify and sever this structure separately. It is always necessary, however, to identify and incise the lateral horn before the levator will come forward freely. A few lobules of the accessory lacrimal gland may prolapse into the wound when the lateral horn is severed.

It will help to understand the various steps of the operation if we try now to visualize what we are going to do.

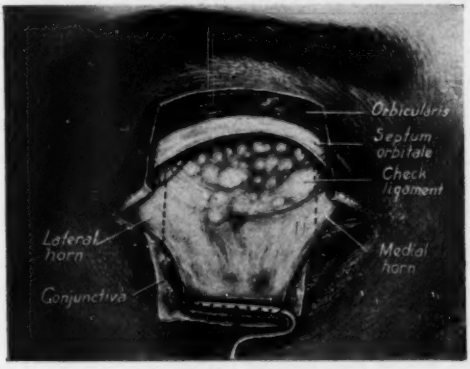

Fig. 4.—Schematic drawing illustrating the position of the levator after it has been freed from the tarsus and pulled downward. Part of the upper lid has been excised to show the deeper structures. Note that the lateral horn, the medial horn, and the check ligament restrict pulling of the levator downward. The dotted lines indicate the site of incision of these structures in freeing the levator muscle during resection of the levator.

The purpose of this operation is to excise *enough* levator tissue to correct the ptosis present. To accomplish this, the levator aponeurosis and Mueller's muscle are grasped with a levator muscle clamp (specially designed for this operation) a few millimeters above the upper border of the tarsus (Fig. 3). After the levator tissues are freed from the tarsus (dotted line, Fig. 3), the muscle clamp is pulled downward and forward. Because the medial and lateral horns are still attached to the levator aponeurosis, these extensions of the levator will restrict the downward or forward movement of the levator (Fig. 4). Also, the nasal part of the check ligament of the levator will limit this movement. Not until these bony attachments of the levator muscle are incised (dotted lines, Fig. 4) will the levator become completely free.

In cutting the check ligament of the levator, one should take care to avoid severing the reflected tendon of the superior oblique muscle, which lies directly below (Figs. 3, 5).

After the above dissection, the levator is easily freed from Tenon's capsule. It is seldom necessary to expose the superior rectus muscle or the reflected tendon of the superior oblique muscle, as illustrated in Figure 5.

Anatomical and Clinical Background for Resection of the Levator Muscle.—This operation is the product of 12 years' study. It was begun with a thorough study of the orbits of several cadavers in the usual three dimensional manner—from in front, from the temporal side, and from above the orbit. This was followed by studies, drawings, and photographs of other cadavers sectioned in the frontal, the sagittal, and the horizontal planes. The study was further extended by resections of the levator on cadavers performed by the Bowman-Wheeler, Blaskovics, and modified Eversbusch techniques. After the operation the heads were frozen, sectioned, and examined to determine the plane of dissection and to learn how much levator tissue had been excised.

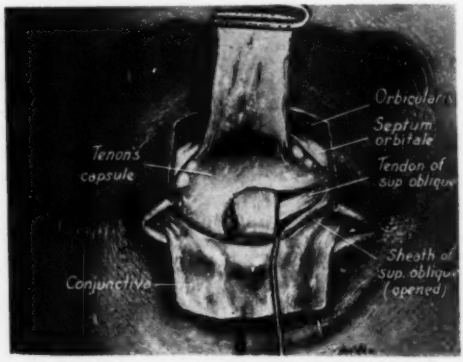

Fig. 5.—Schematic drawing illustrating the relationship of the levator muscle (after it has been freed) to Tenon's capsule, to the superior rectus muscle, and to the reflected tendon of the superior oblique muscle. Tenon's capsule has been opened and part of the upper lid excised to demonstrate these points.

These studies showed that inadequate correction of ptosis following resection of the levator was not due to resection of Mueller's muscle alone (as was sometimes thought) but, rather, to "insufficient resection, pulling out of the sutures or absence of the levator muscle." [6] This cadaver study also explained why the Blaskovics operation gave larger amounts of correction clinically than the Bowman-Wheeler procedure, simply because more levator tissue could be excised in the former procedure.

PREOPERATIVE CLINICAL STUDY

During the past five years data were collected on 109 operations (85 cases), but, of this number, 18 operations (13 cases) had to be eliminated because the follow-up time after operation was less than three months, leaving a total of 91 operations (72 cases) for statistical study.

6. Berke, R. N.: Resection of the Levator Palpebrae for Ptosis with Anatomical Studies, Arch. Ophth. **33**:269-280 (April) 1945.

Of these 72 cases, 6 were acquired and 66 congenital in origin.[7] In 10 of the congenital cases there was a history of ptosis in other members of the family; in 9 other signs of congenital developmental defects were presented, and in 5 external third-nerve paresis was associated with birth trauma.[8] Of the 66 congenital cases, operations for ptosis had previously been done elsewhere in 19, but, in spite of this, they were treated statistically as primary procedures.[9]

The ages of the patients with acquired ptosis varied from 5 to 80 years, with an average age of 33.1 years, while the ages of the group with congenital ptosis varied from 9 months to 54 years, with an average age of 11.75 years and a mean age of 6.5 years. Of the six cases of the acquired type, the ptosis was on the right side in four, being on the left side in two; in none was it bilateral. Of the congenital cases, the ptosis was on the right side in 22, and on the left side in 25, and was bilateral in 19.

Each patient was given a routine eye examination, including refraction when indicated, with special attention to the extraocular-muscle excursions and to measuring the amount of ptosis present when the patient looked up, when he looked straight ahead in the primary position, and when he looked down. An estimate was made of the amount of levator action present by measuring the amount of elevation of the upper lid without frontalis action in looking up from a position of looking down. Because more than half of the patients with congenital ptosis were 6 years old or less, the amount of levator action present sometimes had to be estimated.

The amount of ptosis in the cases of acquired ptosis varied from 3 to 8 mm., with an average amount of 4.8 mm. in the primary position. The amount of ptosis in the cases of congenital ptosis varied from 2 to 8 mm., with an average of 3.8 mm. in the primary position. Therefore, the amount of ptosis in the acquired group averaged about 1 mm. more than that of the congenital group.

Six operations were done in the 6 acquired cases and 85 operations in the 66 congenital cases—7 of the latter being secondary and 78 primary procedures. In 57 of the 78 eyes the superior rectus muscle was normal clinically, and in 21 it was weak.[10]

Of the 57 congenital cases with normal superior rectus function, levator action was good in 56.18% but in only 28.5% of the congenital cases with weak superior rectus muscles was levator function good.[11] This finding was very interesting, for

7. The acquired ptosis followed an operation on the orbit in one case, was associated with neurofibromatosis of the upper lid in one, had developed spontaneously 21 years before in one, followed an injury to the eye in a football game 8 years before in one, developed after ulceration of the cornea 10 years before in one, and followed removal of a benign fibroma of the frontal bone in one.

8. The congenital anomalies were mental retardation, three cases; blepharophimosis, two cases; jaw-winking (Marcus Gunn) phenomenon, two cases; hydrocephalus, one case, and deformities of the heart and spine associated with dwarfism, one case.

9. Five patients had one or more operations utilizing the lifting power of the superior rectus to support the upper lid; 11 had had resections of the levator; 2 had some type of frontalis operation, and 1 had had both a superior rectus and a frontalis type of procedure.

10. There were two cases of blepharophimosis in the former and two cases of the jaw-winking (Marcus Gunn) phenomenon in the latter group.

11. If the upper lid moved upward 6 mm. or more without assistance from the frontalis muscle when the patient looked upward from a position of looking down, the levator was considered to have "good" levator action. If it moved only 3 to 5 mm., the action was considered fair, and if the movement was less than 3 mm. it was considered poor. In very young children function was often impossible to grade the amount of elevation present.

it indicated that the amount of levator action present was determined somewhat by the function of the superior rectus muscle. Also, as will be shown later, it proved to be an important prognostic sign.

OPERATION

The operation to be presented here began five years ago as the classic Blaskovics procedure and was modified as complications and new methods developed.[12] All types of ptosis, favorable or otherwise, were subjected to this procedure to learn its limitations and to test out Blaskovics' contention that his operation gives complete satisfaction "even when the (levator) muscle is absent" because "an apparent function develops even in those cases in which this muscle is completely paralyzed or atrophic." [2]

In every one of these 91 consecutive operations I examined the patient before, during, and after the operation, performing some of the operations myself but assisting in the majority.[13]

The steps of the operation are as follows:

1. The upper lid is retracted upward, the globe pulled down and a 00 plain surgical gut suture placed under the superior rectus muscle. Care should be taken to make sure that the suture is placed under the muscle, not just through Tenon's capsule, and that the reflected tendon of the superior oblique muscle is not also picked up in the suture.[14]

2. The upper lid is then double everted on a Desmarres lid retractor and the conjunctiva undermined and freed from Mueller's muscle. This is best done by blunt dissection with scissors as illustrated in Figure 6.

3. The conjunctiva is then cut free with scissors from its attachment to the upper edge of the tarsus and freed from Mueller's muscle to the upper fornix. Three double-armed 00 plain surgical gut sutures may now be placed through the conjunctiva close to its cut edge and used as traction sutures to assist in this dissection, or these sutures may be inserted later.

4. Mueller's muscle and the aponeurosis are then undermined from the septum orbitale by blunt dissection with scissors, and a levator muscle clamp is applied (Fig. 7).[15]

5. The aponeurosis and Mueller's muscle are then severed from the tarsus (Fig. 8), after which the levator tissues are freed from the septum orbitale by blunt and sharp dissection with scissors to the level of the upper fornix.

6. At this point the lid evertor is removed, the lid turned back to its normal position, and the attachments of the levator to the orbital walls identified. The lateral horn of the levator is located by placing a finger over the external canthal ligament

12. Many suggestions came from the resident and attending staffs.

13. In 21 private cases the postoperative follow-up notes were gathered from the private records of the physician concerned.

14. The superior rectus suture has been intentionally omitted from the drawings illustrating the steps of the operation.

15. A fine hemostat or an extraocular muscle clamp may be used for this purpose, but neither is entirely satisfactory because the handle of the former gets in the way during the later dissection and because the blades of the latter are too short.

while pulling forward on the muscle clamp. A cord-like band will be felt under the skin extending from the lateral aspect of the muscle clamp toward the lateral orbital tubercle. This is later severed.

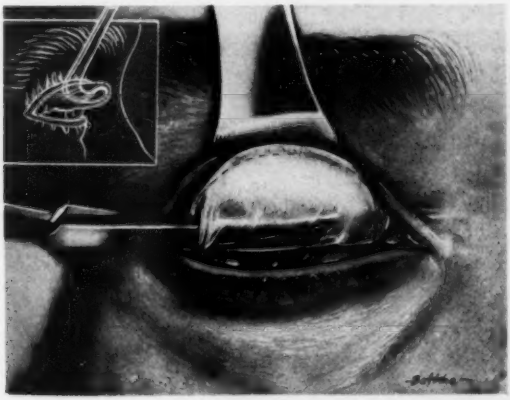

Fig. 6.—The upper lid everted on a lid retractor (see insert); and the conjunctiva undermined with scissors from Mueller's muscle and then freed from the convex edge of the tarsus along the dotted line. The suture under the superior rectus muscle has been intentionally omitted to simplify the illustrations.

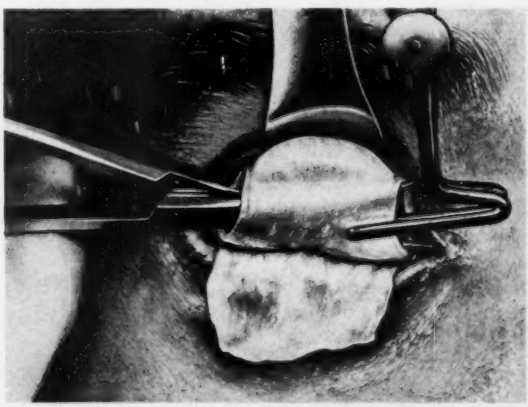

Fig. 7.—The levator aponeurosis, together with Mueller's muscle, undermined with scissors from the septum orbitale and a levator muscle clamp applied to the levator tissues. The conjunctiva has been turned down.

7. The palpating finger is then placed over the pulley of the superior oblique muscle well within the orbit and traction made again on the muscle clamp. The check ligament of the levator will be felt through the skin as a cord-like band extending from the pulley to the medial aspect of the muscle clamp. This also is later severed.

8. At this time one should palpate the superior orbital margin through the skin of the upper lid to determine whether the septum orbitale has been picked up on the clamp. If it has, one will feel a firm band of tissue extending from the clamp to the orbital margin. This must be incised.

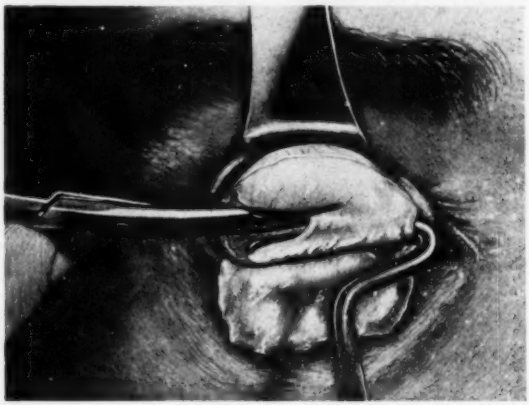

Fig. 8.—The clamp turned downward, and the levator tendon and Mueller's muscle severed from the tissues of the upper lid.

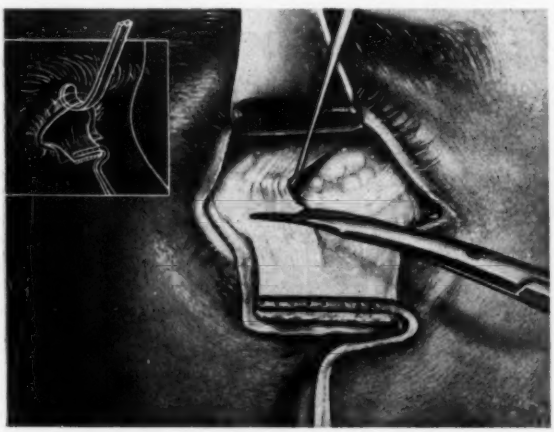

Fig. 9.—The lid retractor removed and the lid turned back to its natural position. The same instrument is then reinserted, this time as a retractor of the upper lid (see insert). If the septum orbitale has been picked up on the clamp, it is lifted up by a muscle hook and freed from the aponeurosis, after which the septum orbitale retracts under the upper lid.

9. The lid retractor is now placed rake-fashion under the upper lid and the latter retracted upward. If the septum orbitale is attached to the levator, the former is incised (Fig. 9).

10. The lateral horn of the levator is then severed by placing one blade of a Stevens scissors under and one blade over the lateral horn and cutting backward toward the apex of the orbit for a distance of 10 to 12 mm. (Fig. 10). After this the lateral aspect of the levator should come forward freely.

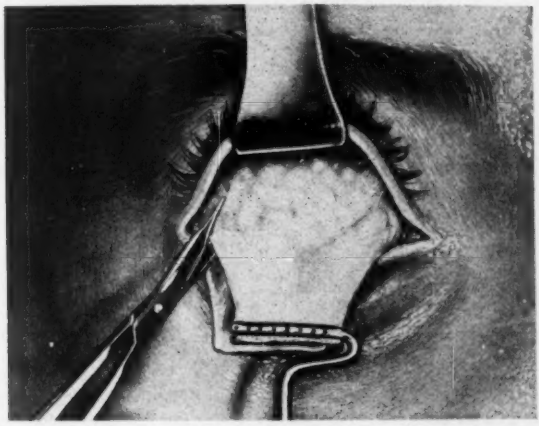

Fig. 10.—The lateral horn of the levator incised with scissors along the dotted line, thus freeing the levator muscle from the lateral orbital wall.

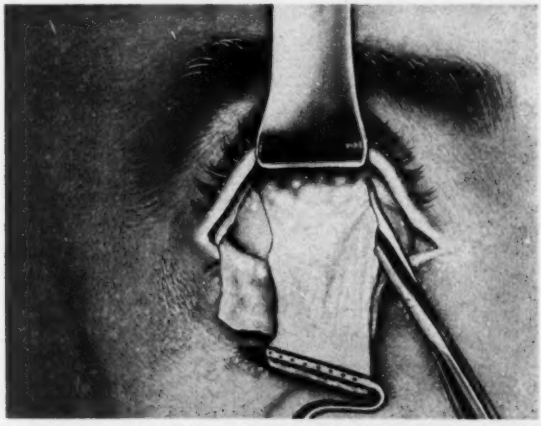

Fig. 11.—The levator muscle freed from the medial orbital wall by cutting the medial horn and the check ligament, as indicated, care being taken to direct the point of the scissors toward the roof of the orbit.

11. The check ligament of the levator is now freed from the pulley. This is done by pulling forward on the levator, placing the two blades of the scissor astride this band, and cutting backward and upward 10 to 12 mm. toward the roof of the orbit parallel with the nasal wall and about 8 to 10 mm. lateral to the pulley

(Fig. 11). After this the entire levator should come forward an additional 10 to 12 mm. If it does not, the lateral and medial attachments have not been completely severed or the septum orbitale is still attached to the levator.

12. In order that it may be determined whether the septum orbitale is attached to the levator, the lid retractor is removed and traction made downward on the

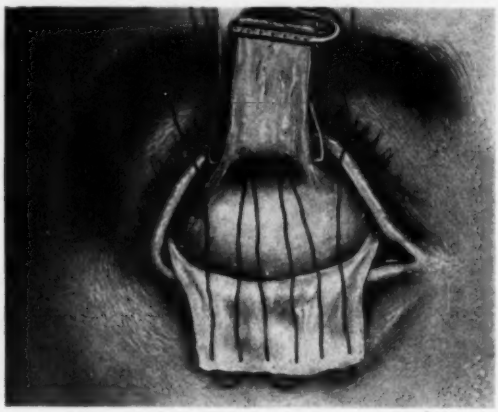

Fig. 12.—Three double-armed 00 plain surgical gut sutures passed through the lower edge of the conjunctiva and then through the levator muscle (which has been freed from Tenon's capsule) as high as possible, so that each suture encircles one-third of the muscle.

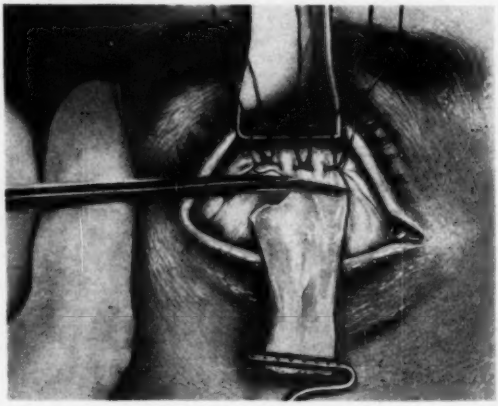

Fig. 13.—Each suture tied with a double knot and the levator muscle excised 2 to 3 mm. in front of the tied sutures.

levator muscle clamp while palpating well within the superior orbital margin. If the septum orbitale is on the clamp, bands of tense tissue will be felt extending from the ptosis clamp to the superior orbital margin. These bands are severed by retracting the lid upward and making a vertical incision through the septum orbi-

tale, bringing into view the upper surface of the levator and the orbital fat. The septum orbitale is then picked up on a muscle hook and completely freed from the anterior, or upper, surface of the levator. If this has been properly done, no more

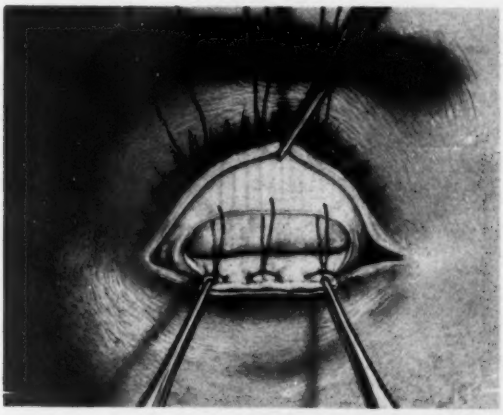

Fig. 14.—One arm of each suture passed through the convex edge of the tarsus to emerge on the skin surface, 4 to 5 mm. above the lashes and 6 to 7 mm. apart. The second arm of each suture is also passed through the lid. These by-pass the tarsus and emerge through the skin 2 mm. above the first sutures.

Fig. 15.—The two arms of each suture spread apart on the anterior surface of the upper lid and a long rubber peg placed on the skin between the two arms, as indicated.

bands to the superior orbital margin should be palpable, and the levator will come well forward. (The septum orbitale is still attached to the levator in Figure 9.)

13. Careful palpation is then done to make sure that the levator has been completely freed from the lateral orbital tubercle, laterally; the pulley of the superior oblique, medially; the septum orbitale, above, and Tenon's capsule, below.

14. If sutures have not already been placed in the conjunctiva, one double-armed 00 plain surgical gut suture is now passed through the middle third of the conjunctiva 2 to 3 mm. from its cut edge, so that the two needles are about 5 mm. apart. Two similar double-armed sutures are also passed through the conjunctiva in like

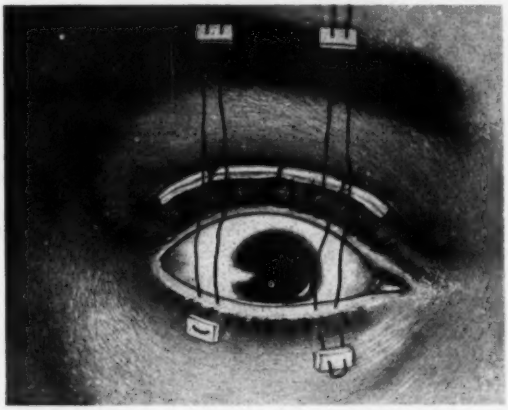

Fig. 16.—Sutures tied over the long rubber peg and the superior-rectus suture (not shown) cut close to the conjunctiva and two modified Frost sutures inserted through the lower lid and anchored to the brow.

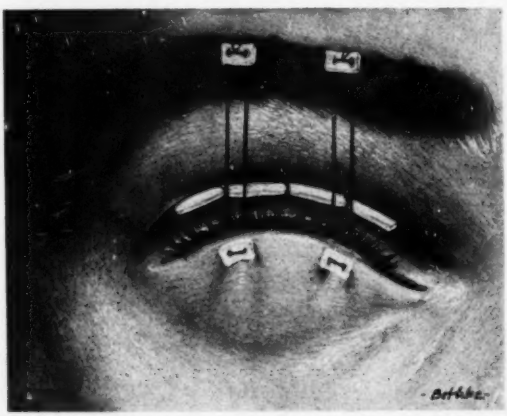

Fig. 17.—Frost sutures tied and lower lid pulled up to act as splint for the upper lid and afford perfect protection for the cornea.

manner on either side of the first suture (Fig. 12). The two needles of the middle suture are then passed through the middle third of the levator as far back as possible and tied on the upper surface of the muscle with a double knot. The other double-armed sutures are then passed through the medial and lateral thirds of the levator muscle at the same level and tied.

15. The levator muscle is then excised 3 mm. in front of the line of sutures (Fig. 13), the lid retractor removed, and the lid pulled downward to its natural position.[16]

16. The upper tarsus is then everted with a fixation forceps and one arm of the central suture passed through the tarsus (1 mm. from its upper border and exactly at the midpoint between the medial and the lateral canthus) and brought out through the skin 4 to 5 mm. from the lashes. The other arm of this suture is passed through the skin 2 mm. above the first suture but missing the tarsus. The other two sutures are passed through the tarsus and the skin in exactly the same manner 7 to 8 mm. on either side of the central suture (Fig. 14).

17. The two arms of each suture are then spread apart, one up over the forehead and one down over the cheek. A long, thin rubber peg, 2 to 3 mm. in diameter and 25 mm. long, is placed on the skin between the two arms of each suture (Fig. 15) and the latter tied firmly with three knots. When tied, these sutures anchor the levator to the tissues of the upper lid, produce a natural-appearing upper-lid fold and support the skin and lashes of the upper lid, thus preventing turning down of the lashes postoperatively.[17]

18. The long ends of the suture in the superior rectus muscle are now cut close to the knot, leaving the knotted suture in place. Two Frost sutures are then passed through the lower lid and then through the deeper tissues of the brow (Fig. 16).[18] When tied, these sutures afford perfect protection to the cornea and support the upper lid (Fig. 17).

19. Penicillin ointment is then placed over all sutures and a firm roller gauze pressure dressing applied for five days.

TECHNICAL COMPLICATIONS DURING OPERATION

Anyone who is not thoroughly familiar with the anatomy of the orbit, or who has never done this operation before, may experience difficulties, chief of which are the following:

1. If the lid evertor is too large, difficulty may be experienced in reflecting the tightly stretched conjunctiva from Mueller's muscle or in reflecting the tense levator aponeurosis from the septum orbitale. Therefore, two sizes of lid evertors should always be available.

2. If a suture has not been placed under the tendon of the superior rectus muscle, the conjunctiva may be dissected beyond the upper fornix and down to the upper limbus. This danger can always be averted by tying a suture in the superior rectus muscle before the operation is begun.

3. In freeing the levator aponeurosis from the septum orbitale, one sometimes inadvertently picks up the latter and reflects it with the former. This complication

16. If the ptosis is more than 4 mm. or if the levator is very thin, it may be advisable to excise with scissors all but the lower 5 mm. of the tarsus.

17. If sufficient levator tissue has been excised or if the levator muscle is not too delicate, the lid should come up to or above the upper limbus with the eye in the primary position. If not, it is advisable to reinsert the sutures farther back in the levator, to perform a tarsectomy, or to do both.

18. Passing these sutures through the gray line of the upper lid may cause distortion of the lashes, with postoperative irritation of the cornea.

occurs in practically every case in which a previous resection of the levator has been done and should be suspected if the levator does not come forward freely after the lateral horn and Whitnall's check ligament have been severed. This complication is easily recognized by palpating the bands of tissue extending from the superior orbital margin to the ptosis clamp. After these bands are freed, the operation usually proceeds smoothly.

4. Occasionally the levator is so delicate that it may tear apart as it is pulled forward. Should this happen, the torn end of the levator is easily picked up on two or three fine hemostats, pulled forward, and placed on the ptosis clamp again.

5. When Whitnall's check ligament is being cut, the reflected tendon of the superior oblique muscle may be accidentally severed if the points of the scissors are directed backward and downward toward the globe, rather than backward and upward toward the roof of the orbit. One such accident occurred in this series, with a resulting overaction of the homolateral inferior oblique muscle.

6. If the check ligament is not completely freed from the pulley, the nasal suture may be passed through this band, causing a notch of the upper lid when the suture is tied. If this is not remedied, a notch of the nasal half of the lid will occur after operation when the patient looks down (Fig. 24). If the reflected tendon of the superior oblique also is picked up on this suture, a peculiar paradoxical elevation of the upper lid will occur after operation when the patient looks down (Fig. 25). These complications can be avoided by completely freeing Whitnall's ligament before passing the sutures through the levator muscle.

7. In cases in which a superior rectus type of operation has already been done, the levator and the superior rectus muscles may be so firmly matted together that the latter is inadvertently severed from the globe with the former. This complication can be recognized by identifying the stump of the superior rectus tendon on the sclera. Should this complication occur, the two muscles must be separated and the superior rectus sutured back to its stump before continuing with the operation.

8. If the levator tears away from the ptosis clamp before the sutures are tied in it, one may accidentally pick up part of Tenon's capsule between the superior rectus and the levator muscles in retrieving the levator. Should this complication occur, it can be recognized by manually rotating the globe up and down while observing the behavior of the levator. If the latter moves up and down with the movements of the globe, Tenon's capsule has been picked up with the levator.[19] Should this occur, the levator must be freed from Tenon's capsule.

POSTOPERATIVE CARE

The pressure dressing and the Frost sutures were usually removed on the fifth postoperative day. The other sutures, tied over the rubber peg and holding the levator, were not removed until the next day if silk had been used, and not at all if plain surgical gut had been inserted.

If the pressure dressing had been firmly applied, usually little or no edema of the lids was present, and one could judge the final result quite accurately. For

19. In one case in which this complication was not recognized until the end of the operation and the error was not corrected the patient had an overcorrection for several months with a good final result. This complication may account for some of Blaskovics' good results when "the levator [was] absent".[2]

example, if the upper lid was at or near the limbus, the final result was usually good or excellent, but if it covered one-half or more of the pupil, the ptosis always remained undercorrected.

If the upper lid covered more than 6 mm. of the cornea at the first dressing, the patient was usually sent home the next day. If it was at or near the limbus, he was kept in the hospital for a few days for observation of the way in which the cornea was going to react to the exposure. Methyl cellulose (0.5%) was ordered every hour during the daytime and the lower lid pulled up over the cornea with cellophane® tape at night to prevent drying of the cornea. If the cornea did not stain after a day or two under this routine, the patient was discharged and advised to continue the same treatment at home until danger of exposure keratitis was over.[20]

FINAL RESULTS OF OPERATION

Ninety-one operations were performed on these 72 patients. The follow-up period varied from 3 months to 5½ years, with an average follow-up of 17 months. An attempt was made to see all patients at least every six months after operation, but this was impossible occasionally because some patients lived at great distances.

The final result was rated on the basis of the last examination, even though the correction for ptosis may have been better at some previous date. To appraise the final result accurately, an arbitrary set of standards was adopted as follows: If the fissures matched so that the upper lids overlapped the two corneas equally in the primary position, the correction was considered "excellent"; if there was a difference of 1 mm., the result was graded "good"; if the difference was 2 mm., the result was called "fair," and if the difference was 3 mm. or more, the result was considered "poor."

To learn what types of ptosis gave the best results, these 91 operations were divided into distinct clinical groups, the amount of correction in millimeters computed for each and the final results compared.

Results in Acquired Versus Results in Congenital Ptosis.—In the six cases of acquired ptosis the ptosis varied from 3 to 8 mm., with an average of 4.8 mm. The amount of levator resection done varied from 12 to 30 mm., with an average of 20 mm. The average amount of correction was 4.3 mm., with an average residual ptosis of only 0.5 mm. In 50% of the group the result was excellent; in 50% there was undercorrection of 1 or 2 mm., and in none of the cases was the result poor (Table 1).

Of the 85 eyes operated on for congenital ptosis, 78 had only one operation and 7 had more than one. In the 78 eyes with congenital ptosis which had only one operation, the ptosis varied from 2 to 8 mm., with an average of 3.8 mm. The amount of resection varied from 15 to 30 mm., with an average of 18.3 mm. The average amount of correction was 2.3 mm. and the average residual ptosis 1.5 mm.

When the amounts of ptosis for the acquired and the congenital groups are compared, it should be noted that the acquired group had 1 mm. more ptosis than the congenital group before operation, and that, despite this difference, the amount of improvement was 2 mm. greater and the residual ptosis 1 mm. less in the

20. In cases with weakness of the superior rectus muscle associated with overcorrection, it was sometimes necessary to follow this routine for two to three months; in other cases two to three weeks sufficed.

acquired group. These figures would tend to indicate that the results of this operation are definitely better in acquired than in congenital ptosis.

When the graded results are compared the difference becomes even more apparent, because in the acquired group there was an excellent result in 50% of cases and not one poor result, whereas in the congenital group the result was excellent in only 39.7% and poor in 21.8%. However, these comparisons are not entirely valid, because the number of cases in the acquired group was too small and because the cause of the ptosis in this group was so varied. Perhaps more cases would have changed the picture entirely.

Results in Congenital Ptosis.—A. PRIMARY OPERATIONS VERSUS SECONDARY OPERATIONS: As mentioned above, 11 patients in this group of 91 operations had

TABLE 1.—*Results in Acquired and Congenital Ptosis*

Type of Ptosis	No. of Operations	Average Mm. of Ptosis			Graded Results							
					Excellent		Good		Fair		Poor	
		Before	After	Improv.	No.	%	No.	%	No.	%	No.	%
Acquired	6	4.8	0.5	4.3	3	50.0	1	16.6	2	33.4	0	0
Congenital (1st operation)	78	3.8	1.5	2.3	31	39.7	17	21.8	13	16.6	17	21.8
Congenital (2d operation)	7	4.0	1.7	2.3	3	42.8	2	28.6	0	0	2	28.6
Total	91	3.9	1.5	2.4	37	40.7	20	21.9	15	16.48	19	20.9

TABLE 2.—*Effect of Superior Rectus Function on Final Result*

Type of Congenital Ptosis	No. of Operations	Average Mm. of Ptosis			Graded Results							
					Excellent		Good		Fair		Poor	
		Before	After	Improvement	No.	%	No.	%	No.	%	No.	%
Normal superior rectus	57	3.6	1.2	2.4	25	43.8	13	22.8	9	15.8	10	17.5
Weak superior rectus..	21	4.4	2.3	2.1	6	28.5	4	19.0	4	19.0	7	33.3
Average	78	3.7	1.5	2.3	31	39.7	17	21.8	13	16.6	17	21.8

had a previous resection of the levator: Of the 11, 7 had had resection of the levator according to the Bowman-Wheeler technique, in which only Mueller's muscle and the aponeurosis were resected; 3, the Blaskovics operation, and 1, an operation of unknown type. These 11 operations were included in the congenital group just discussed rather than being placed in a special group of secondary operations, because I had not personally observed the details of the first operation or determined the cause of failure. However, the final results of the second operation in these 11 cases are known: They were excellent in 7, good in 1, and fair in 3. Therefore it would seem that a previous resection of the levator does not preclude the possibility of getting an excellent result from a second operation.

As shown in Table 1, in 17 of the 78 congenital cases a poor result was derived from the first operation. Six of the 17 patients consented to a second, and 1 to a third, operation. The average amount of ptosis for this group was 4 mm., the amount of correction, 2.3 mm., and the residual ptosis, 1.7 mm. In three (42.8%) cases the result was excellent and in two (28.6%) poor. The poor results in two cases were attributed to failure to find the levator muscle, which had receded too

deeply into the orbit. Of the three cases with an excellent result from a second operation, failure followed the first operation because of insufficient resection in two cases and because of pulling out of the sutures in one case. In these cases the levator was found again in the second operation, shortened and reattached to the upper lid.

From experience in these 7 cases and in the 11 cases in which operation was performed elsewhere, it would seem that a second resection of the levator may be successful if the levator muscle is structurally adequate and has not receded too deeply into the orbit.

B. Normal Superior Rectus Muscle Versus Weak Superior Rectus Muscle: The 78 congenital cases were divided into two groups to learn whether weakness of the homolateral superior rectus muscle was a factor in determining the results of the operation (Table 2).

There were 57 patients with normal and 21 with weak superior rectus muscles. The average amount of ptosis was 3.6 mm. for the former and 4.4 mm. for the latter, while the respective averages for the amount of residual ptosis were 1.2 and 2.3 mm. (Table 2).

These figures show that when the superior rectus muscle was weak in congenital ptosis, the amount of ptosis was greater (4.4 mm. versus 3.6 mm.); moreover, when the superior rectus was weak, the amount of residual ptosis was almost double that present (2.3 mm. versus 1.2 mm.) when the superior rectus muscle was normal (Table 2).

The effect of a weak superior rectus muscle on the end-results is further emphasized by comparing the graded results. For example, when the superior rectus muscle was normal the result was excellent in 43.8% of the cases and was poor in only 17.5%; when this muscle was weak the result was excellent in only 28.5% and poor in 33.3%. In other words, the percentage of excellent results increased when the superior rectus was normal and decreased when it was weak. Therefore weakness of the homolateral superior rectus muscle in congenital ptosis is not a good prognostic sign for resection of the levator.[21]

C. Good Levator Muscle Action Versus Poor Levator Muscle Action: In order that the effect of levator function on the final result might be determined, the group with normal superior rectus muscles and the group with weak superior rectus muscles were each divided into two subgroups according to the degree of levator action present. Then the amount of correction and the final results from operation for each subgroup were compared.

21. Parenthetically, it should be pointed out in this discussion on the cosmetic correction of ptosis that many of these patients had a disfiguring strabismus as well. It is particularly interesting to note that of the group with normal superior rectus muscles only 7.3% had anomalies of the horizontal extraocular muscle (consisting of one case of incomplete third-nerve paresis from questionable birth injury, one case of esotropia, and two cases of exotropia), while the other group, with weak superior rectus muscles, had abnormalities of the horizontal extraocular muscle in 66% (consisting of one case third-nerve paresis from questionable birth trauma, five cases of esotropia, five of exotropia, two patients with the jaw-winking phenomenon of Marcus Gunn, and two eyes with complete external ophthalmoplegia with fibrosis of the superior and inferior rectus muscles). These figures illustrate statistically the variable and complicated nature of ptosis and emphasize that the final cosmetic result is governed as much by the nature of the case as by the skill of the surgeon.

When the superior rectus muscle was normal, the residual amount of ptosis averaged about six times as much when the levator action was poor as when it was good (compare Types 1 and 3, Table 3). Furthermore, when the levator action was good the result was excellent in 56.2% of the patients, but when it was poor an excellent result was obtained in only 35.7%. The degree of levator function present, therefore, was an important factor in determining the end-result.

When the group with weak superior rectus muscles was divided into two subgroups, the significance of good levator action was again emphasized. For example, when the levator action was poor the residual ptosis in millimeters after operation averaged almost four times as much as when the levator action was good (compare Types 2 and 4, Table 3). In other words, 33.3% of the patients with good levator action and weak superior rectus muscles got an excellent result, while only 20% with poor levator action and weak superior rectus muscles derived such a result from this operation.

TABLE 3.—*Effect of Superior Rectus and Levator Muscle Function on Amount of Ptosis, Amount of Correction in Millimeters, and Final Result*

Type of Congenital Ptosis	No. of Operations	Average Mm. of Ptosis			Graded Results							
		Before	After	Improvement	Excellent		Good		Fair		Poor	
					No.	%	No.	%	No.	%	No.	%
1. Normal superior rectus with good levator action	32	3.3	0.4	2.9	18	56.2	7	21.9	6	18.8	1	3.1
2. Weak superior rectus with good levator action	6	4.0	1.0	3.0	2	33.3	1	16.7	2	33.3	1	16.7
3. Normal superior rectus with poor levator action	14	2.9	2.3	1.6	5	35.7	3	21.4	1	7.2	5	35.7
4. Weak superior rectus with poor levator action	10	5.6	3.9	1.7	2	20.0	1	10.0	2	20.0	5	50.0
5. Fair or unrecorded levator action	16	3.8	1.6	1.7	4	25.0	5	31.2	2	12.5	5	31.2
Total	78	3.7	1.5	2.3	31	39.7	17	21.8	13	16.6	17	21.8

The data assembled in Table 3 illustrate some very interesting facts. First, they demonstrate that the functional condition of the superior rectus muscle seemed to determine the amount of levator action present.[22] Second, they show that the amount of ptosis before operation seemed to depend not only on the action of the levator muscle but also on the function of the superior rectus muscle. Third, they indicate that the amount of residual ptosis after operation varied with the function of these two muscles. Fourth, they demonstrate that the best results were obtained when the levator action was good and the superior rectus normal, and the poorest results, when both muscles were weak. These figures emphasize the importance of having good levator action and a normal superior rectus muscle when one is resecting the levator muscle for congenital ptosis.

CAUSES OF UNDERCORRECTION IN CONGENITAL PTOSIS

In the group of 78 primary operations for congenital ptosis, there were 44 cases of undercorrection: In 15 cases this was 1 mm.; in 12 cases, 2 mm., and in 17

22. For example, when the superior rectus was normal only 30.4% of the patients had poor levator action; but when the superior rectus muscle was weak 62.5% of the patients had poor levator action.

cases, 3 mm. or more. (Two cases in which the overcorrection was 1 mm. and one case in which it was 2 mm. were not included here.)

Failure to Overcorrect.—In searching for the causes of these undercorrections, the position of the ptotic lid at the time of the first dressing was studied and compared with the final result. The assembled data in Table 4 shows that the percentage of excellent results varied with the position of the upper lid at the first dressing. For example, when the ptosis was overcorrected at this time, the result was excellent in 70% of the cases, but when the ptosis was undercorrected at the first dressing, the result was excellent in only 8.1%. Also, the position of the upper lid at this time determined the percentage of poor results, for not one of the cases with overcorrection at the first dressing ended in a poor result, whereas, with undercorrection, 43.2% terminated thus.[23] These figures tend to prove that overcor-

TABLE 4.—*Position of Ptotic Lid at First Dressing Versus Final Result*

Position at First Dressing	No. of Cases	Final Result: Excellent No.	Excellent %	Good No.	Good %	Fair No.	Fair %	Poor No.	Poor %
Higher than fellow upper lid	20	14	70.0	5	25.0	1	5.0	0	....
At same level as fellow upper lid	9	4	44.4	3	33.3	1	11.1	1	11.1
Lower than fellow upper lid	37	3	8.1	8	21.6	10	27.0	16	43.2
Position unrecorded	12	10	83.3	1	8.3	1	8.3	0	....
Total	78	31	39.7	17	21.79	13	16.6	17	21.7

TABLE 5.—*Cause of Undercorrection in Congenital Ptosis with Good Levator Action*

Average Position of Lid at End of Operation	No. of Cases	"Fall" of Lid	Final Result: Excellent	Final Result: Undercorrected	Cause of Undercorrection: Insufficient Resection	Poor Levator Tissue	Sutures Failed	Cause Unknown
2.8 mm. above the limbus	4	4.5	2	2	..	..	2	..
Even with the limbus	11	2.4	8	3	2	..	..	1
3.3 mm. below the limbus	6	0.8	3	3	3	..	..	..

rection at the first dressing is the best assurance of ultimate success following this operation, and that undercorrection at this time is the chief cause for failure.

Insufficient Resection.—In order to provide for overcorrection at the first dressing, one must excise enough levator tissue to accentuate the overcorrection at the time of operation, because all ptotic lids tend to "fall" after the operation,[24] the amount of "fall" depending on the amount of overcorrection. For example, in a group of 21 cases with good levator action, the "fall" averaged 4.5 mm. when the lid was raised above the limbus, 2.4 mm. when it was raised only to the limbus, and 0.8 mm. when it was not raised as high as this. The data in Table 5 show that insufficient resection was the main cause of undercorrection when the levator action was good, five of the eight final undercorrections being due to this, two to pulling out of the sutures, and one to an unknown factor.

23. A pressure dressing was used in almost all of these cases to keep down the edema.

24. Only three lids in this series of 91 operations were higher at the first dressing than they were at the end of operation.

Structural Weakness of Levator.—In several cases the levator was so thin and fragile that it tore apart during the operation. In some of these cases it was impossible to raise the lid to the upper limbus. In these cases the result was always undercorrection. In 11 of 15 cases with poor levator function, final undercorrection was attributed to poor levator tissue in seven cases, to insufficient resection in one, to pulling out of the sutures in one, and to an unknown cause in two (Table 6).

In only 5 of these 15 cases was the levator tissue strong enough to support the upper lid at a point averaging 1.8 mm. above the limbus at the end of the operation. In four of these five cases the end-result was excellent. Therefore excellent results may be obtained with resection of the levator with poor levator action if the levator tissues are strong enough to support the upper lid above the upper limbus at the time of operation. In the great majority of these cases, however, the levator was too fragile to accomplish this. From this, we must conclude that structural weakness of the levator muscle is the commonest cause of failure in congenital ptosis when the levator action is poor.

Pulling Out of the Sutures.—Because removal of silk sutures in young children always is an unpleasant experience for both the patient and the surgeon, absorbable

TABLE 6.—*Cause of Undercorrection in Congenital Ptosis with Poor Levator Action*

Average Position of Lid at End of Operation	No. of Cases	"Fall" of Lid	Final Result		Cause of Undercorrection			
			Excellent	Undercorrected	Insufficient Resection	Poor Levator Tissue	Sutures Failed	Cause Unknown
1.8 mm. above limbus.....	5	4.2	4	1	..	1	..	..
Even with limbus.....	4	3.2	0	4	..	2	1	1
2.5 mm. below limbus.....	6	2.7	0	6	1	4	..	1

sutures were preferred. After different kinds of sutures had been tried, it was found that 00 or 000 plain surgical gut sutures were best for this purpose, because these sutures were not absorbed until after the fifth or sixth day.[25]

In 8 of the 44 cases of undercorrection, the result was attributed to failure of the sutures to hold.[26] These cases were characterized by a great "fall" in the position of the upper lid during the time interval between the end of operation and the first dressing. Two factors which favored pulling out of the sutures were postoperative edema of the upper lid and poor function of the levator tissue.

Premature absorption of the gut sutures was not a cause of failure, because there was no essential difference in the final result whether 0000 silk, 0000 plain surgical gut, or 0000 chromic surgical gut sutures were used (Table 7).

Causes for Failure in Congenital Ptosis.—The exact cause of undercorrection in these 44 cases was sometimes difficult to determine because these operations

25. Two-0 plain surgical gut sutures lasted 6 to 7 days; 000 plain surgical gut, 5 to 6 days; 0000 plain surgical gut, 4 to 5 days, and 0000 chromic surgical gut, 10 to 12 days. Five-0 plain, 00000 chromic, and 000000 chromic surgical gut sutures were used in a few cases, but were too fragile. Sutures which lasted longer than six days began to slough out and usually had to be removed.

26. Sometimes it was difficult to decide whether the sutures had pulled out or the levator tissue had stretched.

were performed by many different surgeons (36.6% were done by residents) and because of other inherent, unknown factors concerned. However, the following list is considered a fairly accurate appraisal of the causes of undercorrection: a weak levator muscle, 15 cases; insufficient resection, 19 cases, and pulling out of the sutures or stretching of the levator, 8 cases. In two cases, in which the correction remained excellent for a few months and then gradually changed to undercorrection, the cause was unknown.

When undercorrection occurred in congenital ptosis with good levator action, the cause was generally insufficient resection; when poor levator action was present, the cause was usually inadequate levator tissue; when the sutures failed, the cause was either postoperative edema or poor levator tissue.

To prevent failure with this operation in congenital ptosis, therefore, one should avoid doing this operation in cases with little or no levator action. Enough levator tissue should be excised to produce 2 to 4 mm. of overcorrection at the time of the operation, and a firm pressure dressing should be applied to prevent severe postoperative edema and pulling out of the sutures.

TABLE 7.—*Effect of Different Sutures on Amount of Correction*

Type of Sutures Used	No. of Cases	Average Amount of Ptosis in Mm.		
		Before	After	Improvement
4-0 silk	7	3.8	1.0	2.8
4-0 plain surgical gut	28	3.9	1.1	2.8
4-0 chromic surgical gut	11	3.6	1.1	2.5

AMOUNT OF RESECTION VERSUS AMOUNT OF PTOSIS

In every case an estimate was made of the amount of levator tissue excised.[27] When these measurements were compared with the amount of correction achieved in each case, no correlation could be detected (Fig. 18). For example, one patient with weak levator action derived no correction from a 30-mm. resection in either eye, while two other patients were improved only 1 mm. each by excision of the same amount of levator tissue. In 14 operations, 25 mm. of tissue was excised, with improvement in the ptosis varying from 2 to 8 mm. In 17 other cases, in which 20 mm. of levator tissue was excised, the ptosis was benefited from 1 to 6 mm.; and again in 9 cases, in which 15 mm. of resection was done, the amount of correction varied from 1 to 5 mm. In five other cases of 12 mm. of resection each, the correction varied from 1 to 5 mm. In other words, one could not predict how many millimeters of levator tissue should be excised for 1 mm. of ptosis.

The reason for this discrepancy seems to depend on the nature of the levator tissue excised. As emphasized by Blaskovics, sometimes the levator is nonelastic

27. In some cases this tissue was measured both when stretched and when relaxed, but generally it was impossible to measure accurately the amount of levator tissue excised, even when relaxed, because of the tendency of the excised levator tissue to roll up on itself. If placed on a block, it could be expanded to almost any size, because when spread lengthwise it became narrow crosswise, and when pulled out crosswise it became shorter lengthwise. Therefore measuring the excised tissue when it was relaxed was no more accurate than estimating the amount of tissue resected when it was stretched.

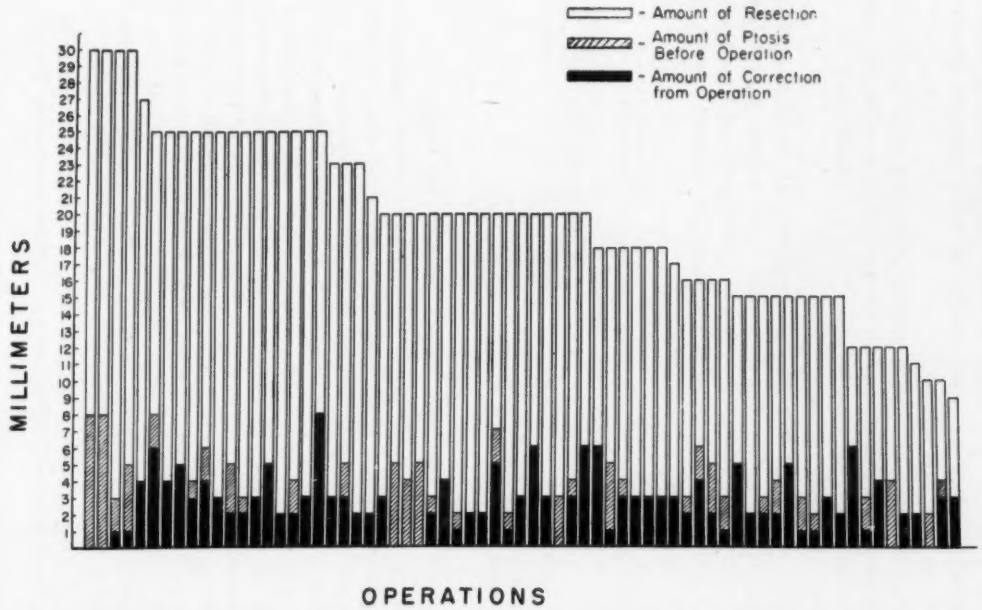

Fig. 18.—Amount of ptosis before operation, amount of levator tissue excised (when stretched), and amount of correction achieved by the operation. Note that there is no correlation between the amount of levator resection and the amount of ptosis correction. Absence of the vertical black bars indicates no correction from the operation; absence of cross-hatched bars indicates no residual ptosis; the difference between the two bars shows the amount of residual ptosis present after operation.

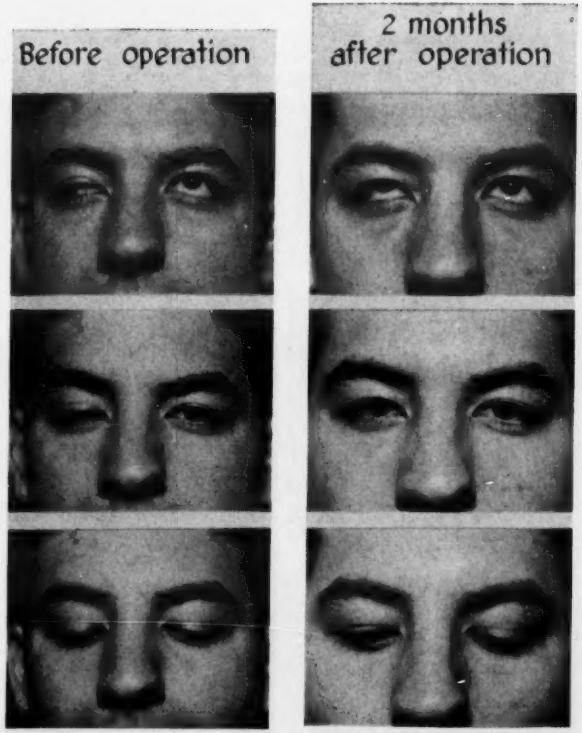

Fig. 19.—Acquired ptosis from injury, with an "excellent" postoperative result. Note the slight postoperative lagophthalmos on the right in looking down. (In all cases an attempt was made to take photographs of the patient looking up, looking straight ahead, and looking down, before and after operation, so that the good and the bad points of the operation might be portrayed.)

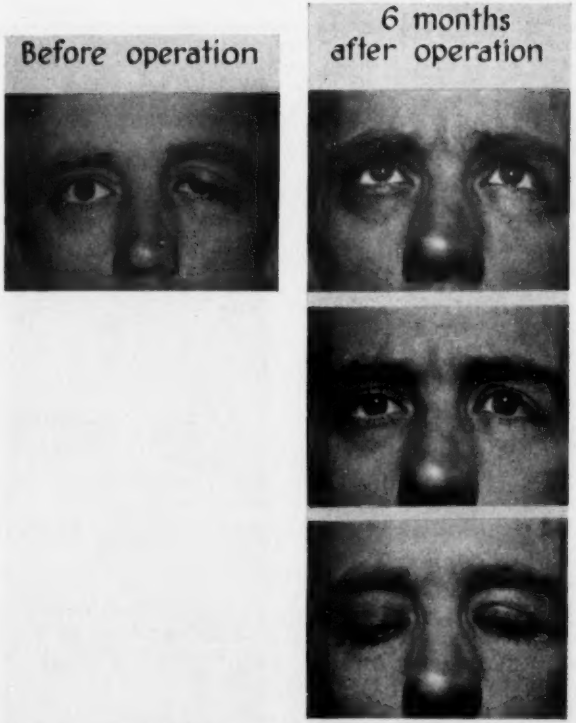

Fig. 20.—Acquired ptosis from neurofibromatosis, with "good" postoperative result (1 mm. overcorrection). Note slight lagophthalmos on left in looking down.

Fig. 21.—Acquired ptosis developing spontaneously 21 years before operation, with "fair" postoperative result (2 mm. undercorrection). Note absence of lagophthalmos in looking down after operation.

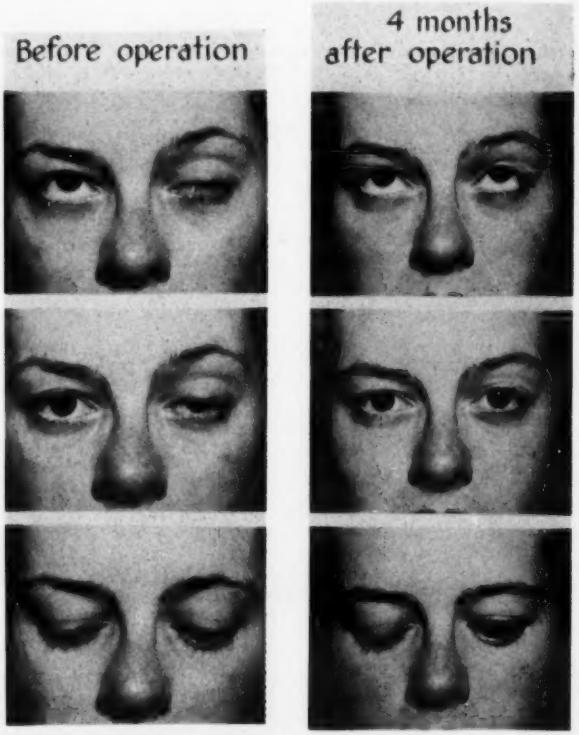

Fig. 22.—Congenital ptosis with "excellent" postoperative result. Note the left lagophthalmos in looking down before and after operation. The left upper lid was 2 mm. above the upper limbus five days after operation.

and fibrous in nature, and sometimes thin, fragile, and easily stretched or torn. For these reasons one cannot formulate a general rule based on so many millimeters of resection for so many millimeters of ptosis.[28]

Blaskovics stated that the amount of resection must be estimated by considering the following eight factors: (1) the elasticity of the levator, (2) the weight of the lid, (3) the length of the fissure, (4) the rigidity of the skin, (5) the presence of epicanthus, (6) the age of the patient, (7) the presence of endophthalmos, and (8) the amount of ptosis present. All these conditions undoubtedly have a bearing

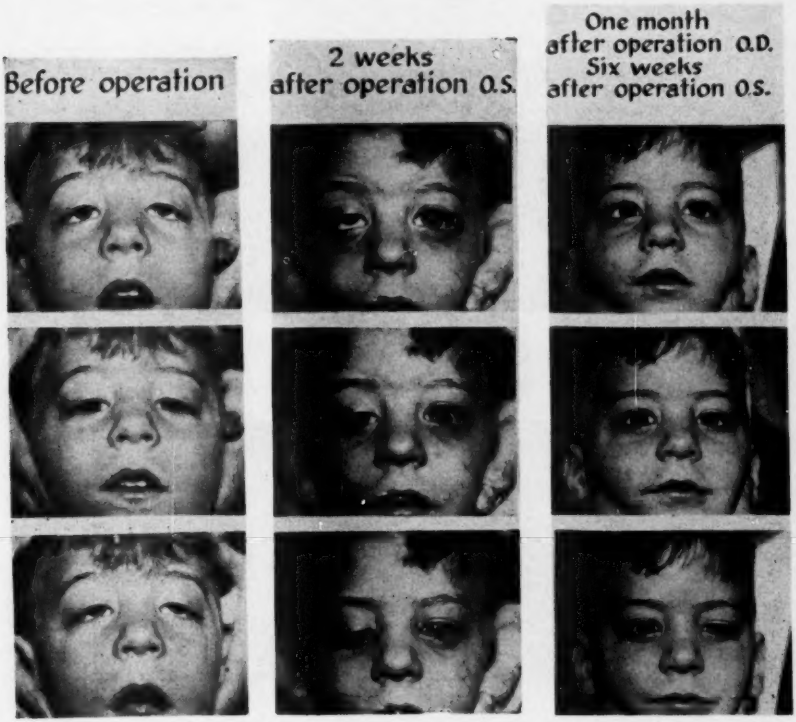

Fig. 23.—Bilateral congenital ptosis with poor levator action and absence of upper lid folds before operation. Note the left lagophthalmos in looking down two weeks after operation and compare with the improvement in the lid lag four weeks later. Right lagophthalmos in looking down disappeared spontaneously later.

on the final result, but accurate appraisal of all these factors seems an impossible task. The only rule which we have found satisfactory in this respect is: Excise enough levator tissue at the time of operation to raise the upper lid to or above the upper limbus.

28. Ever since Wolff (1896) formulated his rule of 1 mm. of levator excision for each millimeter of ptosis, some writers on ptosis have repeated this bit of misinformation. This rule should be discarded because it will nearly always lead to undercorrection, will discredit the operation and will discourage others from trying it.

Fig. 24.—Congenital ptosis associated with third-nerve paresis due to birth trauma. After operation the position of the left upper lid varied from 2 to 3 mm. intermittently, without apparent cause. The photographs do not show the weakness of the left superior rectus muscle.

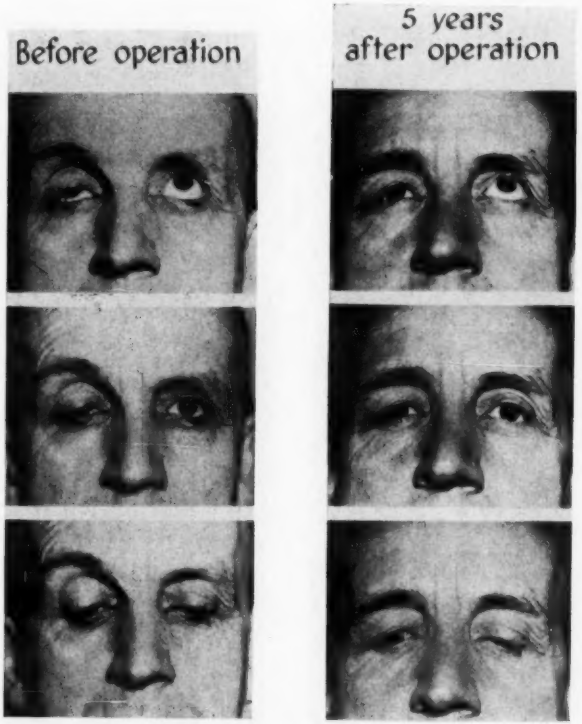

Fig. 25.—Congenital ptosis with a weak superior rectus muscle and poor levator action. Note the right hypotropia in looking up before and after operation, as well as the nasal postoperative lagophthalmos in looking down. The latter resulted from incomplete severance of the check ligament of the levator at operation.

COMPLICATIONS FOLLOWING RESECTION OF THE LEVATOR

The most frequent postoperative complications were (1) temporary overcorrection of the ptosis, (2) mild or severe keratitis, (3) extraocular-muscle imbalances, and (4) lagophthalmos in sleep and in looking down.

Overcorrection.—One of the most welcome "complications" at the first dressing was to find 1 or 2 mm. of overcorrection, because the result in these cases was

Fig. 26.—Bilateral ptosis, greater on the right, with temporary overcorrection and paradoxical elevation of the upper lid in looking down. The latter condition resulted from suturing the superior oblique tendon to the upper lid. Both the overcorrection in the primary position and the bizarre behavior of the upper lid were improved by freeing the superior oblique tendon from the tissues of the upper lid through a skin incision. The patient also had temporary weakness of the right superior rectus muscle after the ptosis operation. (The last photograph was taken two weeks after the superior oblique tendon had been freed.)

usually good or excellent. The duration of the overcorrection lasted from a few days to as long as six months in monocular ptosis. One exception was a case of acquired ptosis from neurofibromatosis in which 1 mm. of overcorrection remained in the primary position seven months after operation (Fig. 20). The only cases

in which overcorrection lasted longer than six months were cases of bilateral ptosis in which only one lid had been operated upon (Fig. 27).[20]

As much as 3 to 4 mm. of overcorrection often corrected itself in a few months (Fig. 27). This spontaneous cure of the overcorrection was attributed to the presence of mild superficial exposure keratitis, which caused a spasm of the orbicularis muscle; this, in turn, stretched the levator so that the overcorrection disappeared. Later, when the overcorrection and the corneal irritation disappeared, the orbicularis spasm also stopped.

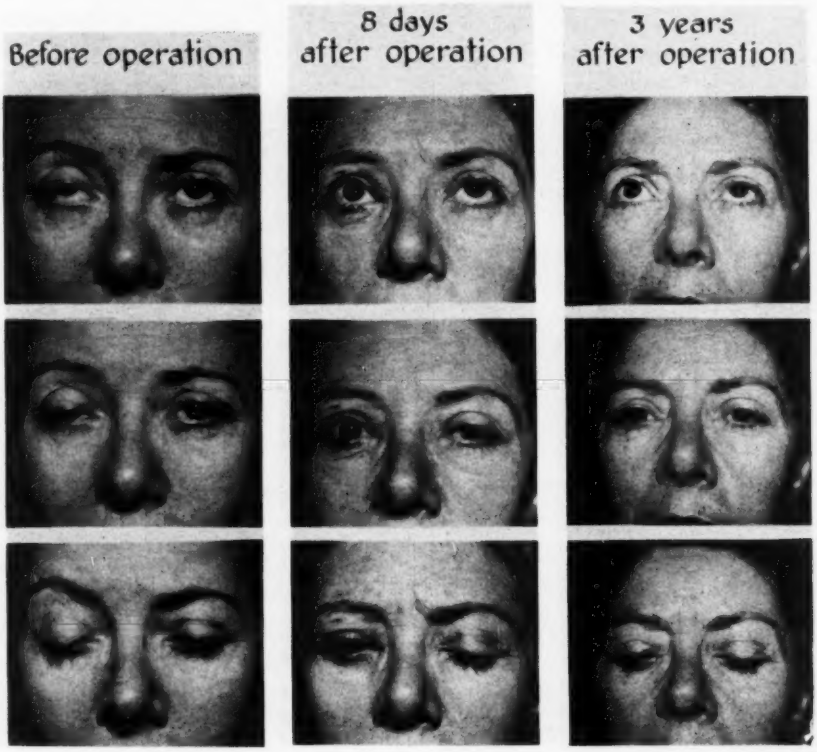

Fig. 27.—Bilateral ptosis, greater on the right, with temporary postoperative overcorrection and lagophthalmos. Note that both the overcorrection in the primary position and the lagophthalmos in looking down had greatly improved spontaneously at the time of the last photograph.

29. Patients with bilateral ptosis of unequal degree were "problem cases" because if we tried to match the less ptotic eye by doing "just the right amount" of resection undercorrection always resulted. If we resected as much of the levator as possible overcorrection sometimes resulted when the positions of the upper lids were compared.

In none of our cases of overcorrection has it been necessary to recess the levator muscle as recommended by Cusick and Sarrail.[30]

Postoperative Keratitis.—After removal of the pressure dressing, for the first few days there was usually some limitation of movement of the upper lid. This relatively fixed position of the lid, plus the fact that the cornea had never before been completely exposed to air, predisposed to injury to the epithelium, especially in cases in which the superior rectus muscle was weak, so that superficial staining

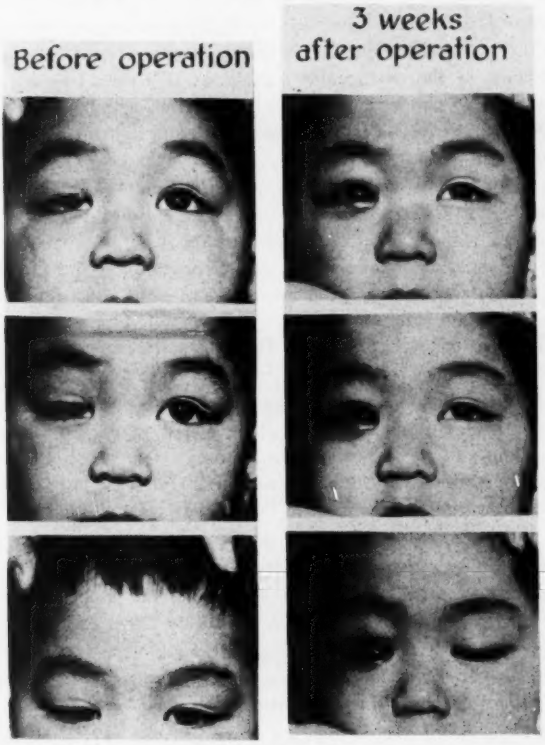

Fig. 28.—Postoperative corneal scar from corneal irritation of inturned eyelashes. The ulceration healed soon after epilation of the offending lashes, and the lagophthalmos in looking down became less with time.

of the cornea with fluorescein was usually present for a few days. If methylcellulose was ordered every hour, this staining usually disappeared. If staining persisted, covering the cornea with the lower lid caused prompt healing in 8 to 12 hours. Only when this precaution had been omitted, or when the eyelashes turned in to irritate the cornea, did deep keratitis occur.

30. Cusick, P., and Sarrail, J. A.: Blepharoptosis: Modifications of Blaskovics Procedure, Its Indications, Management of Its Complications, Kresge Eye Inst. Bull. **2**:38-45 (Nov.) 1945.

In three cases the Frost sutures were inserted through both the upper and the lower lid margins, causing the lashes of the upper lid to grow downward and scratch the cornea after operation. In one of these cases this complication was not recognized for several days, as a result of which a corneal ulcer involving the substantia propria, with subsequent scarring, resulted (Fig. 28). In all three cases the ulceration healed soon after the lashes had been epilated. In another case necrosis and sloughing of the cornea presented at the time of the first dressing. In this case only one Frost suture had been inserted, which had pulled out under the dressing, thereby allowing the lashes to come in contact with the exposed cornea.

Extraocular Muscle Anomalies Induced by the Operation.—Soon after the Frost sutures had been removed, the lower lid usually assumed its normal position. Testing for weakness of the extraocular muscles at this time was not entirely satisfactory, especially in children, because of the edema and tenderness of the parts. In several cases, however, temporary limitation of movement was noted, especially in looking up or in looking down.

In three cases weakness of the superior rectus muscle persisted, at least to some degree, for as long as a year after the operation. In another case there was a marked overaction of the homolateral inferior oblique muscle, presumably from accidental tenotomy of the superior oblique at the time of operation. In a fifth case, in which a slight hyperphoria had been noted before the operation, estropia associated with hypertropia developed after operation. This complication was not the result of injury to either the superior oblique or the external rectus muscles, as was proved by operation later.

Because of the difficulty in examining the superior rectus muscle before operation in the presence of ptosis, it cannot be stated with certainty that the postoperative weakness of the superior rectus muscles reported here was entirely the result of the operation. However, I am fairly certain that this deformity was caused by the operation in at least two cases, even though no direct visible injury occurred to the superior rectus muscles at the time.

Postoperative Lagophthalmos.—Before operation several patients with congenital ptosis presented marked limitation of motility of the upper lid, characterized by ptosis in upward gaze and lagophthalmos in looking down (Fig. 22). This limitation of motility naturally persisted after operation and accounted for the persistence of ptosis in these patients in looking up and of lagophthalmos in looking down, even though no ptosis was present in the primary position.

Sometimes lagophthalmos in looking down affected only the nasal half of the upper lid (Fig. 25). In these cases a band of tissue could be felt under the skin extending from the tarsus toward the pulley of the superior oblique muscle—the result of not completely freeing the levator and of inserting the nasal suture through Whitnall's check ligament at the time of operation. This complication can be avoided by completely freeing the levator from its attachment to the pulley.

In two cases the reflected tendon of the superior oblique muscle was accidentally caught in the nasal suture and anchored to the tissues of the upper lid. This resulted in a bizarre paradoxical elevation of the upper lid in downward gaze (Fig. 26). The condition was corrected by freeing the tendon from the upper lid through a skin incision.

Lagophthalmos in looking down (Figs. 19 to 28) and in sleep was often present for months after the operation, but in time this tended to become less (Figs. 23, 27).

CASE REPORTS ON RESECTION OF THE LEVATOR MUSCLE

The following case reports are typical of the final results for the different types of ptosis reported above.

CASE 1.—*Acquired ptosis with excellent result.*

A man aged 24 was struck in the right eye 8 years before during a football game, after which the right upper lid began to droop. Examination showed 7 mm. of ptosis of this lid in looking up, 3 mm. in the primary position and 1 mm. of lagophthalmos in looking down (Fig. 19). In October, 1946, a 17-mm. resection of the levator was done with the patient under general anesthesia, with an "excellent" result.

CASE 2.—*Acquired ptosis with good result.*

In a man of 28 drooping of the left upper lid developed in association with neurofibromatosis. In October, 1946, an 18-mm. resection of the levator was done, with a "good" result, that is, with 1-mm. overcorrection (Fig. 20).

CASE 3.—*Acquired ptosis with fair result.*

A woman aged 41 stated that the right upper lid had begun to droop spontaneously 21 years before. Examination showed 9 mm. of ptosis of the right lid in looking up, 8 mm. in the primary position and 6 mm. in looking down. In May, 1946, a 25-mm. resection of the levator muscle was done, with a "fair" result—2 mm. of undercorrection (Fig. 21).

CASE 4.—*Congenital ptosis with normal superior rectus muscle and good levator action; excellent result.*

A girl of 14 came to Dr. John H. Dunnington, having had ptosis of the left upper lid since birth. Examination showed 7 mm. of ptosis in eyes up, 5 mm. in eyes straight and 1 mm. of lagophthalmos on the left in eyes down. In June, 1945, a 15-mm. resection of the levator muscle was done, with an "excellent" final result (Fig. 22).

CASE 5.—*Bilateral congenital ptosis with normal superior rectus muscles and weak levator action; excellent result.*

A boy aged 2½ had been born with bilateral ptosis; this caused him to hold his chin up in order to see straight ahead in the horizontal plane. In April, 1950, a maximum resection of the levator muscle was done on the right eye, and four weeks later a similar operation on the left eye, with an "excellent" result (Fig. 23) in each eye.

CASE 6.—*Congenital ptosis with weak superior rectus muscle and good levator action; fair result.*

An 8-year-old boy came to see Dr. John H. Dunnington because of a drooping left upper lid following instrument delivery at birth. When he was 4 years old, a resection of the levator had been done elsewhere, with little or no improvement. Examination showed incomplete paresis of the left third cranial nerve with weakness of the left superior rectus muscle and ptosis. The ptosis measured 8 mm. in looking up, 6 mm. in the primary position, and nothing in looking down. In May, 1946, the left levator muscle was resected 16 mm., with a "fair" result, or with 2 mm. of residual ptosis (Fig. 24).

CASE 7.—*Congenital ptosis with weakness of the superior rectus muscle and poor levator action; fair result with nasal lagophthalmos.*

A man of 43 came to Dr. John H. Dunnington with congenital ptosis of the right upper lid. Examination showed 8 mm. of ptosis in looking up, 5 mm. in the primary position, and 1 mm. of lagophthalmos on the right in looking down. In addition, the right superior rectus muscle was weak. In March, 1946, a 23-mm. resection of the right levator muscle was performed, with a "fair" result, that is, with 2 mm. of residual ptosis. Figure 25 shows weakness of the right superior rectus muscle before and after operation and nasal notching of the upper lid in looking down after operation.

CASE 8.—*Bilateral congenital ptosis; overcorrection following second operation, with paradoxical elevation of upper lid.*

A girl of 7 years had had drooping eyelids since birth, the ptosis being greater on the right side. In July, 1949, and again in September, 1949, a resection of the levator was done.

After the last operation, overcorrection of the ptosis and a peculiar paradoxical elevation of the upper lid developed when the patient looked down (Fig. 26). This condition was later corrected by freeing the reflected tendon of the superior oblique muscle from the tissues of the upper lid through a skin incision.

CASE 9.—*Congenital ptosis with overcorrection, which "cured" itself.*

A woman aged 49 had bilateral congenital ptosis. The ptosis on the right measured 4 mm. more than that on the left with the eyes in the primary position. In December, 1947, a 15-mm. resection of the right levator muscle was performed, with temporary overcorrection (Fig. 27), which later almost completely disappeared spontaneously.

CASE 10.—*Congenital ptosis; second operation resulting in corneal ulceration from inturned eyelashes.*

A 3-year-old Chinese boy had from birth a right ptosis of 4 to 5 mm. An 18-mm. resection of the levator in June, 1946, resulted in undercorrection. A second operation, in January, 1947, temporarily overcorrected the ptosis and caused the lashes to turn in against the cornea. The resulting corneal ulcer healed after the offending lashes had been epilated (Fig. 28).

SUMMARY

A brief review of the anatomy of the upper lid showed that the levator palpebrae muscle is attached to (1) the tissues of the upper lid via Mueller's muscle and the levator aponeurosis, (2) the lateral orbital tubercle via the lateral horn of the levator, (3) the pulley of the superior oblique via Whitnall's check ligament, (4) the septum orbitale above, and (5) the conjunctiva and Tenon's capsule below. These attachments must be identified and severed in the operation of resection of the levator muscle for ptosis.

A simplified Blaskovics type of operation for shortening the levator muscle which has the following advantages is presented: 1. Reflection of the conjunctiva can be done more easily and with less bleeding. 2. The levator aponeurosis is more easily and certainly reflected from the septum orbitale. 3. A ptosis clamp is used to hold the levator securely, thus dispensing with an extra set of sutures. 4. A more certain method for freeing the levator from the lateral orbital tubercle, the pulley of the superior oblique, and the septum orbitale is presented. 5. One set of sutures, instead of two, is used to anchor the levator to the tissues of the upper lid. 6. The sutures are fixed to the upper lid so as to produce a natural-appearing upper lid fold, to support the skin of the upper lid, and to turn the eyelashes up and away from the cornea. 7. A safer method is suggested for covering the cornea after operation, the lower lid also acting as a splint to the upper lid. 8. A firm pressure dressing is recommended to prevent postoperative edema and pulling out of the sutures.

The results of operation in 91 patients, followed from three months to 5½ years, are presented. It is shown that the amount of correction was better in a group of six cases of acquired ptosis than in a group of 85 cases of congenital ptosis. The results of operation on the latter group varied with the function of the superior rectus, as well as with the amount of levator muscle action present. The best results occurred in patients with good levator action and normal superior rectus muscles; the poorest, in patients with poor levator function and weak superior rectus muscles.

Successful correction of the ptosis depended on achieving overcorrection at the time of the first dressing. Final undercorrection was attributed mainly to

inadequate resection, to the presence of poor levator tissue, or to pulling out of the sutures. Permanent overcorrection was rare except in cases of bilateral ptosis in which only one lid had been corrected.

Formulation of a rule of so many millimeters of resection for so many millimeters of ptosis was impossible because of the variable structure of the levator muscle in ptosis. The simplest and most reliable rule was found to be: Excise enough levator tissue to raise the ptotic lid up to or above the upper limbus.

When the first operation failed, a second was sometimes successful if the levator could be found.

Complications following the operation were (1) temporary overcorrection, (2) temporary superficial keratitis, (3) occasional extraocular muscle anomalies, and (4) slight lagophthalmos in looking down.

Members of the staff of Presbyterian Hospital cooperated in the collection of these data.

Registry of Interesting Cases

It is the purpose of this section to record cases on the basis of interest only. No complete review of the literature is attempted and no claim for priority is implied except when specifically stated. Publication of case reports is subject to the concurrence of the Editorial Board on the interesting aspects of the case. It is requested that the reports submitted be as brief as is consistent with inclusion of the pertinent facts, bear a title that is as specific as possible, be prefaced by a paragraph that states why the author feels the case is of interest and be accompanied with photographs whenever possible.

ADENOCARCINOMA OF THE LID, SECONDARY TO ADENOCARCINOMA OF THE STOMACH

This case is interesting enough to be presented, first, because the lesion was twice removed as an ordinary chalazion, when recurrences prompted a pathologic study, and, second, because adenocarcinoma of the stomach with metastasis to the lids is extremely rare.

A white man aged 70 was seen in the department of ophthalmology of the Straub clinic (formerly The Clinic) with what appeared to be a chalazion of the right upper lid. The lesion was excised and the patient followed for one week, at the end of which time he was discharged as cured, with no evidence of the presence of the original mass. One week after this, the mass recurred in the same area. Curettement was resorted to at this time. One week later, however, when the mass recurred on the lid margin, complete excision and curettement were done, and the

Fig. 1.—Lid lesion prior to last surgical removal.

material was sent to the department of pathology (Fig. 1). The diagnosis returned was metastatic adenocarcinoma (Fig. 2).

Further investigation of the patient's medical history revealed that four months previously he had had a gastric resection for suspected adenocarcinoma of the stomach and that at the present examination he had metastases to the liver. The pathologic diagnosis of adenocarcinoma of the stomach was made from material obtained at operation (Fig. 3). In view of the patient's past history and the recent findings, further surgical intervention was not considered, and he was given 1,600 r to the involved lid area; this treatment did not affect the lesion in any way. The patient died on Nov. 21, 1951. Permission for autopsy was refused.

A portion of the specimen was sent to Dr. Merrill J. Reeh; it was sectioned and studied in the Weeks Memorial Laboratory of the University of Oregon Medical School. The diagnosis arrived at there was "adenocarcinoma of the right upper eyelid, metastatic, from adenocarcinoma of the stomach (well differentiated)."

The sections were shown also to members of the American Ophthalmologic Pathology Club, and it was their opinion that the tumor of the eyelid was of the same type as that of the stomach, and that it had reached the lid by metastasis.

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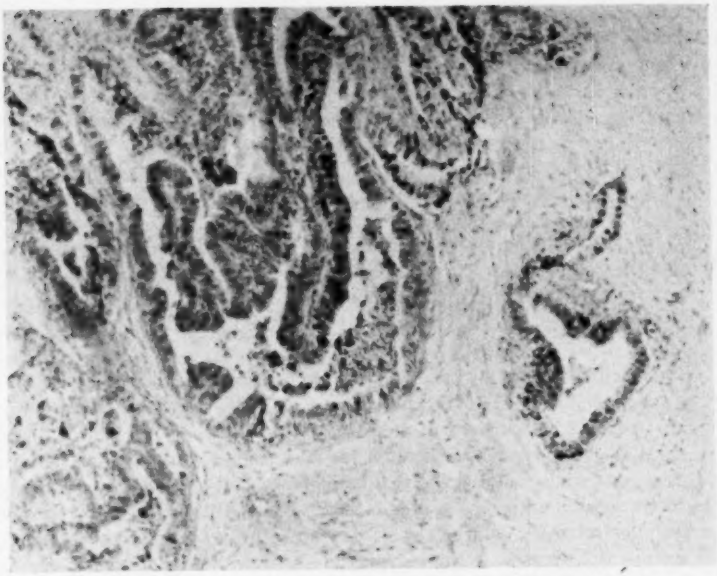

Fig. 2.—Photomicrograph of metastatic adenocarcinoma of the lid.

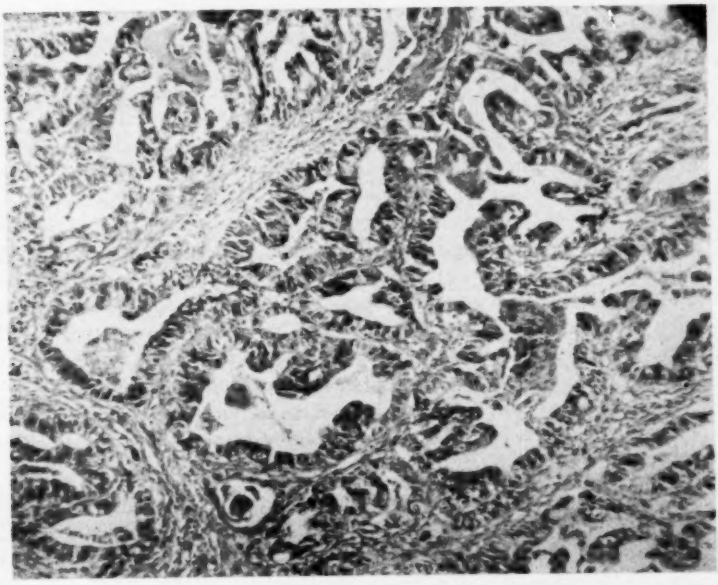

Fig. 3.—Photomicrograph of primary lesion in the stomach.

Annual Reviews

PHYSIOLOGIC CHEMISTRY OF THE EYE

A Review of Papers Published During 1951

V. EVERETT KINSEY, Ph.D.
DETROIT

AS IN PREVIOUS years, papers chosen for review include not only those which deal directly with the chemistry of various parts of the eye but also some concerned with related subject matter.

CORNEA

Succinic dehydrogenase was demonstrated to be present in the cornea by staining with tetrazonium blue.[1] The enzyme is present in higher concentrations in the epthelium than in other portions of the cornea.

In an elaborate investigation, Maurice [2] determined quantitatively in living rabbits the permeability of the limiting membranes of the cornea to sodium and discussed the results with regard to the Cogan-Kinsey theory [3] that the cornea is maintained in a relatively deturgesced state by loss of water to the tears and aqueous humor, owing to differences in osmotic pressure between these fluids and the cornea.

Maurice administered Na^{24} by instillation in the conjunctival sac and by intravenous and intraocular injections. From the rates at which Na^{24} accumulated and from the steady-state ratios of activity, he calculated the permeability constant for the corneal epithelium in the direction in-out and for the endothelium in the direction aqueous humor to cornea. The values were 0.00080 to 0.0024 cm. per hour for the epithelium and 0.072 cm. per hour for the endothelium. From differences in the rates of accumulation of Na^{24} in the central and peripheral portions of the cornea under various conditions, Maurice concludes that about five times as much sodium exchanged across the endothelium as exchanged between the blood stream and the periphery of the cornea. The resistance of the stroma to diffusion of sodium was about eight times the value in free solution.

The permeability of the blood-aqueous and cornea-aqueous (endothelium) barriers, when determined after direct intraocular injections, was two to three times normal. Maurice's observation that the permeability of the blood-aqueous barriers to sodium increases after the eye is punctured is consistent with that of other investigators, who have observed a similar effect of intraocular injections.

The permeability constant which Maurice reports for the epithelium, it should be noted, really represents both the epithelium and the conjunctiva overlying the sclera, since the test fluids were in contact with the entire corneal-conjunctival-palpebral

From the Kresge Eye Institute.

1. de Berardinis, E.: Research Concerning Succinic Dehydrogenase in Ocular Tissues, Boll. Soc. ital. biol. sper. **27**:1336, 1951.

2. Maurice, D. M.: Permeability to Sodium Ions of the Living Rabbit's Cornea, J. Physiol. **112**:367, 1951.

3. Cogan, D. G., and Kinsey, V. E.: The Cornea: V. Physiologic Aspects, Arch. Ophth. **28**:661, 1942.

cul-de-sac. In an attempt to show that the Na^{24} entered the aqueous humor chiefly across the cornea, Maurice blocked off most of the corneal surface with a thin colloidin cap lightly greased with petrolatum U. S. P. ("vaseline") and noted that the activity of the center of the cornea was reduced to less than that obtained in the absence of the cap, while the ratio of the aqueous humor-cornea activity maintained its proper value. Use of the vacuum technique devised by Cogan,[4] which makes it possible to overlay only the cornea, or a selected portion thereof, with a solution, would seem to provide a more direct method of determining the permeability constant for the epithelium alone.

Maurice points out that his results would be compatible with the theory of deturgescence based on differences in osmotic pressure only if the endothelium were impermeable to chloride ions, a possibility which he considers unlikely in view of its permeability for sodium. He suggests that there is an active transport of some ion, possibly but not necessarily sodium, across the endothelium of the cornea to the aqueous humor, a hypothesis which would seem to be supported by recent work of Potts and Johnson [5] on the ability of other ions (P^{32}, Na^{24}, I^{131}, Cs^{134}) to penetrate the cornea.

Maurice considers the possibility of excretion of water directly from the cornea, but points out that this process would be the least efficient energetically of all methods of keeping the cornea in a relatively dehydrated state.

In view of the anatomical and chemical similarity of the epithelium and stroma of the cornea and the same portions of the ciliary body, it occurs to the reviewer that the same secretory mechanism may be operative in both tissues, i. e., that the primary ion secreted is bicarbonate [6] and that the transfer of other ions is controlled by the amount of bicarbonate which is secreted.

Assuming the correctness of the idea that ions are actively transported out of the cornea, water would be transferred across the limiting membrane (as it is thought to be in the ciliary body) as a result of osmotic forces, as originally suggested in the Cogan-Kinsey theory. However, the important contribution of Maurice, and Potts and Johnson is their evidence of an active transport of ions, which ions, as Davson [7] points out, might otherwise accumulate subepithelially if water only were lost from the cornea, and thus abolish the difference in osmotic pressures between the stroma and its surrounding fluids, the tears and the aqueous humor. Furthermore, their work indicates that a part of the energy required for the transfer of water out of the cornea comes from the cornea itself, as well as from evaporation of tears and the secretory activity of the ciliary body.

The critical experiment to determine whether movement of ions across the epithelium and endothelium is a result of secretory activity, viz., by investigating whether enzyme poisons will diminish or abolish the movement, remains to be performed.

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4. Cogan, D. G., and Hirsch, E. O.: The Cornea: VII. Permeability to Weak Electrolytes, Arch. Ophth. **32**:276, 1944.

5. Potts, A. M., and Johnson, L. V.: Nutritional Supply of Corneal Regions in Experimental Animals: I. Supply of Some Inorganic Ions, Am. J. Ophth. **33**:405, 1950.

6. Kinsey, V. E.: A Unified Concept of Aqueous Humor Dynamics and the Maintenance of Intraocular Pressure, Arch. Ophth. **44**:215, 1950.

7. Davson, H.: Some Considerations on the Salt Content of Fresh and Old Ox Corneae, Brit. J. Ophth. **33**:175, 1949.

The electrical resistance of the cornea is reported to reside in the limiting membranes, the epithelium and endothelium, rather than in any stroma-epithelium bond.[8] Storage at room temperature, immersion in organic liquids, and surface-analgesic solutions, which lead to structural alterations in the epithelium, resulted in a decrease in resistance.

It is generally believed that the cornea does not swell appreciably after cornea-stripping procedures. In rabbits, at least, the cornea does swell after removal of the epithelium. Maurice and Giardini [9] found that the average initial rate of increase in thickness in vivo after removal of the epithelium was about 0.5% per minute. It was 2% and 3% per minute after removal of the endothelium and endothelium together with Descemet's membrane, respectively. The cornea swelled to about twice its normal size after removal of the epithelium and remained at this thickness for about two days; it then regained its original thickness after one or two days more.

The possibility of a causal relation between the transparency of the cornea and the imbibition properties of the collagen and mucoid of the stroma was investigated by van Walbeek and Neumann.[10] Previous investigators have shown that transparency of the cornea is dependent upon its content of water, which in the living animal is regulated by the epithelium and endothelium. Van Walbeek and Neumann show that swelling of the cornea in acid solutions can be accounted for on the basis of swelling of collagen, whereas in basic solutions it is due to swelling of mucoid. They point out that the maximal transparency of the cornea occurs when the amount of water is from two to four times the weight of the dry material, i. e., is the same concentration approximately as that found in fresh corneas. They showed that mucoid is precipitated by acid and extracted by alkali, that in solutions of either acids or bases the cornea becomes clouded, and they conclude that mucoid is necessary for corneal transparency. They suggest the existence of a complex relation between collagen and mucoid. Their statement that the cornea swells less in salt solutions than in water should be questioned in view of earlier observations [11] which indicate that the rate of swelling, but not the extent, is less in salt solutions than in water, so that the relative amount of swelling is dependent upon the time at which the observation is taken.

The difference in transparency of the cornea and the sclera was again correlated with the degree of hydration.[12]

Various criteria which have been used in the past to judge the suitability of various methods of storing corneal pieces for transplantation were cited in detail

8. Katzin, H. M.: A Study of the Electrical Resistance Properties of Corneal Epithelium, Am. J. Ophth. **34**:1159, 1951.

9. Maurice, D. M., and Giardini, A. A.: Swelling of the Cornea in Vivo After the Destruction of Its Limiting Layers, Brit. J. Ophth. **35**:791, 1951.

10. van Walbeek, K., and Neumann, H.: Studies of Corneal Transparency Under Various Experimental Conditions, A. M. A. Arch. Ophth. **46**:482, 1951.

11. Kinsey, V. E., and Cogan, D. G.: The Cornea: III. Hydration Properties of Excised Corneal Pieces, Arch. Ophth. **28**:272, 1942.

12. Winkelman, J. E.: Difference Between Corneal and Scleral Connective Tissue, Ophthalmologica **122**:107, 1951.

by the late Dr. Wilhelm Buschke.[13] He stressed particularly the criteria which take into account swelling properties of the cornea. He showed that when the whole eye was stored in the cold, the water content of the cornea increased significantly as soon as eight hours after death of the animal; progressive hydration of the cornea during cold storage in a moist chamber was shown to be due predominantly to the uptake of fluid from the interior of the eye itself. From experiments in which corneas were suspended over solutions of sodium chloride of various concentrations at the temperature conventionally used for cold storage, it was concluded that at this temperature vapor pressures over salt solutions of concentrations less than 0.5 m are not in equilibrium with the forces determining hydration or deturgescence of the cornea. In addition to swelling of the cornea as a whole, which in vivo may be controlled by a balance of osmotic forces operating across the intact epithelium and endothelium, Buschke called attention to the "hydropic" swelling of the stromal cells and suggested that these cells have an essential function in fluid elimination which may be impaired under the aphysiologic condition of cold storage.

Some correlation seems to exist between hydration of corneas during cold storage and susceptibility to autolysis on subsequent incubation at higher temperatures.[14] The amount of total nonprotein nitrogen and ammonia nitrogen increased in corneas of whole eyes which were stored in the cold for three days and then incubated. No increase in these nitrogen fractions was observed in fresh corneas or corneas stored under conditions which excluded hydration. Injection of a 0.005 or 0.02 m solution of sodium fluoride prior to incubation resulted in an increase in amount of nonprotein nitrogen.

Arginine, histidine, and cysteine applied locally to the eye increased the rate of cicatrization of superficial and deep corneal wounds of the rabbit; asparagine, phenylalanine, glutamine, tryptophan, and proline were less effective.[15] The respiratory rate of the cornea was observed to increase in the presence of cysteine, histidine, arginine, asparagine, and phenylalanine. The healing action, the authors believe, very probably depends on the action of amino acids on the oxidative processes of the cornea.

The use of antibiotic derivatives of Actinomycetes in concentrations employed clinically was not found to reduce the rate of repair of small epithelial defects in the cornea of rats.[16] The eyes were removed and placed in test solutions for three hours. The pH was maintained at 7.2 by use of a phosphate buffer. Penicillin in concentrations as great as 50,000 units per milliliter and bacitracin in concentrations of 1,000 units per milliliter retarded healing. Benzalkonium (zephiran®) chloride and benzethonium (phemerol®) chloride (organic antiseptics), as well as butacaine (butyn®) sulfate, tetracaine hydrochloride, 2% pilocarpine nitrate and fluorescein sodium prevented healing.

13. Buschke, W.: Studies on Experimental Corneal Storage: Bibliographic Survey; Observations on Water Uptake in Corneal Stroma Cells, Am. J. Ophth. **34**:153 (May, Pt. 2) 1951.

14. Buschke, W.; Howard, A., and Siegel, L.: Nitrogen Fractions as Criterion of Preservation of Corneal Tissue, A. M. A. Arch. Ophth. **45**:27, 1951.

15. de Berardinis, E., and Bonavolontà, G.: Healing Activity of Some Amino Acids on Experimental Corneal Lesions and Their Influence on Corneal Metabolism, Gior. ital. oftal. **4**:86, 1951; abstracted, Ophth. Lit. **5**:390, 1951.

16. Marr, W. G.; Wood, R., and Storck, M.: Effect of Some Agents on Regeneration of Corneal Epithelium, Am. J. Ophth. **34**:609, 1951.

The administration of cortisone subconjunctivally in rabbits with homologous corneal grafts also produced a delay in wound healing and prevented keratoblastic proliferation but did not inhibit proliferation of the epithelium.[17]

DeRoetth [18] made an investigation of the glycolytic activity of the cornea. He used as a measure of glycolytic activity the amount of lactic acid which accumulated in solutions in which corneas were incubated. He found that under anaerobic conditions all parts of the cornea produced lactic acid, but under aerobic conditions no more lactic acid accumulated in flasks containing the whole corneas than in those containing the corneas lacking the epithelium. In the case of the stroma the rate of anaerobic production of acid was the same as the aerobic production of acid. The investigator concluded that the stroma possessed both aerobic and anaerobic glycolysis, whereas the epithelium exhibited anaerobic, but no aerobic, glycolysis. The statement that the epithelium possessed no aerobic glycolysis is not justified without further evidence and would seem to result from a misunderstanding of the dynamic nature of glycolysis. This misunderstanding occurs so frequently in the literature and involves such a basic concept that a short discussion of the principles involved would seem to be justified.

Glycolysis is the breakdown of glucose to pyruvic and lactic acids; the breakdown occurs either in the presence of oxygen (so-called aerobic glycolysis) or in its absence (anaerobic glycolysis). In neither case does oxygen participate directly in the reaction; hence glycolysis is an anaerobic process. The usual methods of measuring glycolytic activity (and those employed by deRoetth) consist in determining directly (by chemical analysis) or indirectly (from carbon dioxide liberated from the medium) the amount of lactic acid which accumulates. Under anaerobic conditions lactic acid is not further oxidized by tissues, and hence the quantity of accumulated lactic acid is a measure of the rate of anaerobic glycolysis. Under aerobic conditions, however, lactic acid, in the presence of suitable enzymes is further metabolized, in part at least, through the Krebs cycle to carbon dioxide and water, so that the amount of accumulation of lactic acid represents the difference between the amount of acid produced and that which is oxidized or lost in some other manner; hence, it is not a measure of the rate of aerobic glycolysis.

Since it is well known that the lens epithelium uses oxygen, i. e., possesses respiratory activity, it seems likely that the lack of additional lactic acid from the epithelium under aerobic conditions in deRoetth's experiments can be accounted for as readily by any of the alternative mechanisms suggested above as by lack of formation, as implied by deRoetth. The experiment on the stroma indicates that this portion of the cornea does not metabolize lactic acid, i. e., possesses no respiratory activity, an observation compatible with that of Herrmann and co-workers [19] that the stroma, in contrast to the epithelium, does not utilize oxygen.

Further evidence that the cornea utilizes oxygen directly from the air and that oxygen diffuses through the living cornea in both directions is presented.[20]

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17. Newell, F. W., and Dixon, J. M.: Effect of Subconjunctival Cortisone upon the Immediate Union of Experimental Corneal Grafts, Am. J. Ophth. **34**:977, 1951.

18. deRoetth, A., Jr.: Glycolytic Activity of the Cornea, A. M. A. Arch. Ophth. **45**:139, 1951.

19. Herrmann, H., and Hickman, F. H.: Further Experiments on Corneal Metabolism in Respect to Glucose and Lactic Acid, Bull. Johns Hopkins Hosp. **82**:260, 1948.

20. Langham, M.: Respiration of the Cornea, J. Physiol. **115**:65, 1951.

Studies on chick embryos indicate that respiration in both the cornea and the lens decreases from the 12th day to birth and that glycolysis diminishes slowly up to the 14th day.[21] The rates of both respiration and glycolysis in these tissues, however, are greater in the newborn than in the adult.

Various papers dealing with the metabolism and nutrition of the cornea are reviewed by Cogan [22] in an article chiefly concerned with the applied anatomy and physiology of this structure.

AQUEOUS HUMOR

The chemical composition of all the substances which contribute appreciably to the osmotic pressure of the aqueous humor and arterial plasma of rabbits, as well as the osmotic pressure and hydrogen ion concentration of these fluids, is reported by Kinsey.[23] The data were presented in last year's review,[24] since they appeared in part in an article published in 1950.

Interest has continued to center around the rate of flow of aqueous humor. Grant [25] made continuous recordings of intraocular pressure with an electric tonometer and computed the flow rate in normal and in glaucomatous eyes. He concluded that the increase in intraocular pressure in glaucoma is probably caused exclusively by increased resistance to outflow, and not by any increase in the rate of production of aqueous humor. The average net rate of flow in normal eyes was 2.4 cu. mm. per minute (range, 1.1 to 5.3 cu. mm. per minute), or 0.22 cu. mm. per minute per millimeter Hg intraocular pressure. The rate of flow in glaucomatous eyes tended to be slightly less than normal (1.8 cu. mm. per minute), and the "facility of outflow" varied from essentially zero to about 0.10 cu. mm. per minute per millimeter Hg intraocular pressure, depending, in part, on the type of glaucoma.

The rate of flow in normal eyes, as estimated by the rate of loss of fluorescein, is shown by Goldmann [26] to be 2.2 cu. mm. per minute. In cases of simple glaucoma the rate decreased slightly to 1.7 cu. mm. per minute. These values are essentially identical with those reported by Grant.

In contrast to Grant, Goldmann reports that in cases of chronic congestive glaucoma with elevated tension the rate of flow was increased above normal. Goldmann conceived of the rate of flow as equal to the outflow pressure divided by the resistance between the anterior chamber and the veins of the episcleral lamina. About three-fourths of the resistance he found to be represented by resistance of the corneoscleral trabecula, and one-fourth of the resistance, to outflow through the vessels out of Schlemm's canal.

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21. de Vincentiis, M., and Auricchio, G.: Metabolism of the Cornea and Lens During Embryonal Life, Rass. ital. ottal. **20**:69, 1951; abstracted, Am. J. Ophth. **34**:1772, 1951.

22. Cogan, D. G.: Applied Anatomy and Physiology of the Cornea, Tr. Am. Acad. Ophth. **55**:329, 1951.

23. Kinsey, V. E.: Chemical Composition and Osmotic Pressure of the Aqueous Humor and Plasma of the Rabbit, J. Gen. Physiol. **34**:389, 1951.

24. Kinsey, V. E.: Physiologic Chemistry of the Eye: A Review of Papers Published During 1950, A. M. A. Arch. Ophth. **46**:441, 1951.

25. Grant, W. M.: Clinical Measurements of Aqueous Outflow, A. M. A. Arch. Ophth. **46**:113, 1951.

26. Goldmann, H.: Outflow Pressure, Minute Volume, and Resistance of Aqueous Flow in Man, Docum. ophth. **5**:278, 1951.

Using the paraaminohippuric-acid method,[27] Bárány [28] determined the rate of flow of aqueous humor in the White Leghorn chicken and found that it was 1.7 and 2% per minute of the volume of the anterior chamber.

Bárány [29] also made determinations of the rate of flow of aqueous humor in the normal and in the scorbutic guinea pig in order to ascertain whether the ascorbic-acid-dependent dye-transport mechanism described by Friedenwald [30] is responsible for the production of the bulk of the aqueous humor. On the assumption that the substance used to determine the flow rate, viz., paraaminohippuric acid, did not diffuse across the blood-aqueous barriers, Bárány computed the following rates: animals saturated with ascorbic acid, 1.9% per minute; control animals, 1.7% per minute; moderately scorbutic animals, 1.9% per minute; severely scorbutic animals, 1.4% per minute. Bárány concluded that the data do not support the thesis that the bulk production of aqueous humor is dependent upon the concentration of ascorbic acid in the plasma. The slight decrease in rate of flow of aqueous humor in the severely scorbutic animals could readily be accounted for on the basis of tissue damage.

Becker, Linné and Bárány [31] found that the turnover rate of ascorbic acid in the aqueous humor of rabbit eyes is 1.3 to 1.5% per minute. They used a method which utilizes the fall and rise in the concentration of this substance after alternate occlusion of the carotid arteries. This observed rate appears to be slightly higher than the rate of flow of aqueous humor in the rabbit (1.1% per minute [32]) and suggests that some ascorbic acid is lost by diffusion from the aqueous humor of the anterior chamber.

Harris and Gehrsitz [33] investigated the relationship of the steady-state ratios of xylose and arabinose and the plasma concentrations of these substances in rabbits and cats. They report that in the rabbit the steady-state ratio increased from approximately 0.25 to approximately 0.65 in the plasma-concentration range of 2 to 5 mM./per kilogram of water, respectively, and increased slightly with higher plasma concentrations. Little change in the steady-state ratio was observed with varying plasma concentrations of xylose and arabinose in the cat.

The steady-state ratio of ascorbic acid in the cat is normally unity or above. According to Langham,[34] this ratio decreased to less than unity when the blood level of ascorbic acid was elevated by injection of this vitamin. Langham concludes from

27. Bárány, E., and Kinsey, V. E.: Rate of Flow of Aqueous Humor: I. Rate of Disappearance of Para-Aminohippuric Acid, Radioactive Rayo[illegible] and Radioactive Diodrast from the Aqueous Humor of Rabbits, Am. J. Ophth. **32**:177 (June, Pt. 2) 1949.

28. Bárány, E.: Rate of Flow of Aqueous Humor in the Chicken, Acta physiol. scandinav. **22**:340, 1951.

29. Bárány, E.: Rate of Flow of Aqueous Humor in Normal and Scorbutic Guinea Pigs, A. M. A. Arch. Ophth. **46**:326, 1951.

30. Friedenwald, J. S., and Stiehler, R. D.: Circulation of the Aqueous: A Mechanism of Secretion of the Intraocular Fluid, Arch. Ophth. **20**:761, 1938.

31. Becker, B.; Linné, E., and Bárány, E.: Rate of Turnover of Ascorbic Acid in Aqueous Humor in Rabbits, A. M. A. Arch. Ophth. **45**:653, 1951.

32. Kinsey, V. E., and Bárány, E.: Rate of Flow of Aqueous Humor: II. Derivation of Rate of Flow and Its Physiologic Significance, Am. J. Ophth. **32**:189 (June, Pt. 2) 1949.

33. Harris, J. E., and Gehrsitz, L. B.: The Aqueous: Plasma Steady State Ratios; Their Variation and Significance, Am. J. Ophth. **34**:113 (May, Pt. 2) 1951.

34. Langham, M.: Secretion and Rate of Flow of Aqueous Humour in the Cat, Brit. J. Ophth. **35**:409, 1951.

this observation that the entry of ascorbic acid is determined (as in the rabbit) by active transfer when the concentration in the blood plasma is low and by diffusion when the plasma concentration is high. The steady-state ratio of cysteine was shown to be less than unity and independent of plasma concentration, from which the author concludes that this amino acid enters the aqueous humor by diffusion.

On the basis of the same reasoning as that employed by the American workers [35] in formulating a general theory of aqueous-humor dynamics, Langham concludes that the relative deficiency of both ascorbic acid and cysteine indicates that there is a bulk flow of aqueous humor in the cat eye. This apparently means that the general concept of aqueous-humor dynamics has been accepted by a member of the group which once denied its validity.[36]

Langham employed the basic equations given by Kinsey and co-workers [37] to compute values for the rate of flow of aqueous humor in the cat. The calculated values were from 1 to 2% per minute, depending upon the assumptions made as to the nature of the fluid replacing that lost by bulk flow. In effect, the lower value was calculated on the assumption that the test substances entered solely by diffusion, and the higher value, on the assumption that they entered by secretion. In view of the experimental evidence cited by Langham, it would seem that the lower value is much nearer the correct one.

Further knowledge concerning the nature of the blood-aqueous barriers and the properties affecting the rate of penetration of compounds into the aqueous humor was derived from studies of the rates of penetration of different classes of substances under normal conditions and after the administration of various pharmacologic agents. Ross [38] showed that rapidity of penetration of a series of monosubstituted thiourea derivatives correlated positively with their lipid solubility, as expressed by the ether-water partition coefficient. This worker found that the rate of penetration of compounds across the blood-aqueous barriers did not depend upon molecular volume, or on chemical structure other than that which affected lipid solubility, of the test substance. The selective permeability of the blood-aqueous barriers, Ross thought, resulted from the selective affinity of the membranes of the barrier for lipid-soluble substances, so that these substances could more readily penetrate through the cells than through water-filled pores of limited size between the cells. The dependence of the rate of penetration on lipid solubility also appears to apply to some antibiotics. Langham [39] showed that, of the antibiotics in common clinical use, chloramphenicol, whose lipid solubility is greater than that of the penicillins, penetrated the blood-aqueous barriers most readily.

35. Kinsey, V. E., and Grant, W. M.: (*a*) Mechanism of Aqueous Humor Formation Inferred from Chemical Studies on Blood-Aqueous Humor Dynamics, J. Gen. Physiol. **26**:131, 1942; (*b*) Secretion-Diffusion Theory of Intra-Ocular Fluid Dynamics, Brit. J. Ophth. **28**:355, 1944.

36. Duke-Elder, S., and Davson, H.: Significance of Distribution Ratio of Non-Electrolytes Between Plasma and the Intra-Ocular Fluid, Brit. J. Ophth. **27**:431, 1943.

37. Kinsey and Bárány.[32] Kinsey and Grant.[35a]

38. Ross, E. J.: Transfer of Non-Electrolytes Across the Blood-Aqueous Barrier, J. Physiol. **112**:229, 1951.

39. Langham, M.: Factors Affecting the Penetration of Antibiotics into the Aqueous Humour, Brit. J. Ophth. **35**:614, 1951.

There is considerable evidence, however, that lipid solubility is only one of the factors which determine the rate of penetration. For instance, Davson [40] showed that the rates of penetration of monosaccharides, nitrogen compounds, such as urea, creatinine, aminoacetic acid, and alanine, and various sulfonamide derivatives are independent of lipid solubility.

Both cysteine and cystine were shown by von Sallmann and co-workers [41] to pass into the aqueous humor from the blood stream. Incidentally, the intravenous injection of relatively large amounts of cysteine prior to x-irradiation afforded some protection against cataract.

Palm [42] reports that the barrier to the penetration of sodium into the aqueous humor is the capillary wall which lies between the capillary blood and the tissue fluid of the anterior uvea. He observed, too, that sodium in the anterior chamber of the rabbit was renewed at a rate of about 1% per minute—a value in agreement with that reported previously.[32]

The permeability of the blood-aqueous barriers was not altered by the subconjunctival or retrobulbar injection of hyaluronidase,[43] nor was it affected by daily parenteral administration of corticotropin to normal subjects, as measured by the Amsler and Huber fluorescein test.[44]

The permeability of the blood-aqueous barriers in 10 of 13 eyes which showed clinical manifestations of inflammation was decreased upon administration of cortisone.[45] This substance, when administered subconjunctivally, can be recovered from the aqueous humor.[46]

Both anoxia [47] and prolonged luminous stimulation [48] accelerated the passage of fluorescein across the blood-aqueous barriers. It was postulated that the increased permeability resulting from exposure to light was caused by the liberation of histamines or acetylcholine.

Von Sallmann and Locke [49] report that the blood-aqueous barriers are more permeable after x-irradiation.

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40. Davson, H.: The Penetration of Some Sulphonamides into the Intra-Ocular Fluids of the Cat and Pabbit, J. Physiol. **110**:416, 1950.

41. von Sallmann, L.; Dische, Z.; Ehrlich, G., and Munoz, C. M.: Study on Penetration of Cysteine and Cystine into the Aqueous Humor of Rabbits and Its Relation to Early X-Irradiation Effects on the Eye, Am. J. Ophth. **34**:95 (May, Pt. 2) 1951.

42. Palm, E.: Passage of Radioactive Sodium from the Blood to the Ciliary Body and the Aqueous Humor, Acta ophth. **29**:269, 1951.

43. Morpurgo, F.: Hyaluronidase and Hemato-Ophthalmic Permeability, Ann. ottal. e clin. ocul. **77**:425, 1951; abstracted, Am. J. Ophth. **35**:604, 1952.

44. Cook, C., and MacDonald, R. K.: Effects of Cortisone on the Permeability of the Blood-Aqueous Barrier to Fluorescein, Brit. J. Ophth. **35**:730, 1951.

45. Simonelli, M., and Calamandrei, G.: Behavior of the Blood-Aqueous Barrier After Administration of ACTH, Gior. ital. oftal. **4**:340, 1951.

46. de Berardinis, E., and Bonavolontà, G.: Passage and Concentration of Cortisone in the Aqueous Humor, Boll. Soc. ital. biol. sper. **27**:1336, 1951.

47. Giardini, A., and Swanljung, H.: Effects of Anoxia on the Fluorescein Permeability of the Blood-Aqueous Barrier, Brit. J. Ophth. **35**:114, 1951.

48. Bottino, C.: Blood-Eye Barrier and Luminous Stimuli, Ann. ottal. e clin. ocul. **77**:281, 1951; abstracted, Am. J. Ophth. **34**:1770, 1951.

49. von Sallmann, L., and Locke, B. D.: Experimental Studies on Early Lens Changes After Roentgen Irradiation: II. Exchange and Penetration of Radioactive Indicators (Na^{24}, K^{42}, I^{131}, P^{32}) in Normal and Irradiated Lenses of Rabbits, A. M. A. Arch. Ophth. **45**:431, 1951.

The effect of transient alterations in constituents of the blood on the intraocular pressure was studied by Takagi.[50] After an injection of 10% sodium chloride into the carotid arteries of rabbits, the intraocular pressure rose rapidly to more than 40 mm. Hg; it changed little after injection of 50% glucose. Distilled water similarly administered produced a slight rise in pressure, and isotonic sodium chloride solution produced no change. Injection of a solution of 10% sodium chloride and 50% glucose apparently increased the permeability of the blood-aqueous barriers to fluorescein.

LENS

Zeller, Daily, and co-workers report the presence of adenosinetriphosphatase, pyrophosphatase, 5-nucleotidase, and *l*-peptidase in the lens.[51] The activity of these enzymes was partially reduced in cataract and in the presence of glutathione or ascorbic acid. Exposure of lenses to microwaves reduced the activity of pyrophosphatase only when the intensity of the radiation was sufficient to produce grossly visible evidence of damage.[52] No reduction in activity of adenosinetriphosphatase or pyrophosphatase was noted in the circumscribed posterior cortical cataract which developed after exposure of the eyes to microwaves. The activity of both these enzymes was greatly diminished in completely cataractous lenses. The loss of activity after exposure to microwaves presumably resulted from heat denaturation, since both pyrophosphatase and adenosinetriphosphatase are particularly heat-labile and since the irradiation was shown to raise the intraocular temperature to from 47 to 54 C.

Pirie [53] found that the capsule of the lens contains some hexosamine and a protein which is similar to collagen except that it contains about 10% carbohydrate. The carbohydrate component consists of glucose and a small amount of galactose.

The enzyme systems which function in the oxidative breakdown of carbohydrates in the lens are postulated by Kinsey and Frohman [54] to be the same as those which are known to function in other tissues, namely, the cytochrome and riboflavin systems. Ely,[55] in a previous paper, reports that the addition of cytochrome c to lens homogenates increased the rate of oxidative utilization of various intermediates in the tricarboxylic-acid cycle but was unable to demonstrate the presence of cytochrome c in the lens. Kinsey and Frohman [54] later found that cytochrome c was present in the lens, but only in the epithelium, where it exists in relatively high concentration (approximately 200 mg. per 100 gm.). These workers also report the presence of

50. Takagi, Y.: Experimental Studies on the Intra-Ocular Pressure, Influenced by the Intracarotid Injection of a Hypertonic Solution (Saline and Glucose), Acta Soc. ophth. jap. **55**:132, 1951; abstracted, Ophth. Lit. **5**:538, 1951.

51. Zeller, E. A.; Daily, L., Jr.; Wakim, K. G., and Herrick, J. F.: Contribution to the Enzymology of the Normal and Cataractous Lens, Proc. Staff Meet., Mayo Clin. **26**:194, 1951.

52. Daily, L., Jr.; Zeller, E. A.; Wakim, K. G.; Herrick, J. F., and Benedict, W. L.: Influence of Microwaves on Certain Enzyme Systems in the Lens of the Eye, Am. J. Ophth. **34**:1301, 1951.

53. Pirie, A.: Composition of Ox Lens Capsule, Biochem. J. **48**:368, 1951.

54. Kinsey, V. E., and Frohman, C. E.: Studies on the Crystalline Lens: IV. Distribution of Cytochrome, Total Riboflavin, Lactate, and Pyruvate, and Its Metabolic Significance, A. M. A. Arch. Ophth. **46**:536, 1951.

55. Ely, L. O.: Oxidation of Lactic Acid, Pyruvic Acid, and Various Members of the Citric-Acid Cycle by Bovine Lens Homogenates, Am. J. Ophth. **34**:127 (May, Pt. 2) 1951.

riboflavin, the prosthetic group of the flavoprotein enzyme system; this substance is distributed as follows: epithelium, 0.28 mg.; cortex, 0.003 mg., and nucleus, less than 0.00006 mg. per 100 gm. The ratio of the concentration of lactate to pyruvate was found to be only 0.05 in the epithelium, whereas it was 25 and 12 in the cortex and nucleus, respectively.

The ratios of lactate to pyruvate indicates that the cytochrome and riboflavin systems in the epithelium are functioning in the oxidation of carbohydrates, and not solely in the oxidation of amino acids or fats. Thus, the postulate that some unusual type of oxidative enzyme system is present in the lens [56] is unnecessary. The relatively high ratios of lactate to pyruvate and the lack of evidence of cytochrome c in the cortex and nucleus are indicative of a strictly anaerobic type of metabolism. Since oxidative reactions yield approximately 16 times as much energy per mole of glucose utilized as do glycolytic reactions, the possibility is suggested that one function of the epithelium may be to provide energy for the other portions of the lens, presumably in the form of high-energy phosphate compounds, such as adenosinetriphosphate.

Cataractous human lenses removed from cadavers from 6 to 18 hours after death are reported by Kahan [57] to contain no riboflavin, whereas clear lenses similarly obtained were found to contain 0.0 to 7.7 γ of riboflavin per gram of lens.

Sobagski [58] reported that in embryonic chicken lenses the rate of respiration at the start of incubation was high and the rate of glycolysis was low. At the time of rapid differentiation (seventh to ninth day) the relation of the rates was reversed. The rates became constant after 30 days' incubation.

The suggestion that ascorbic acid may be synthesized by the lens was first made by Müller [59] in 1934. During the intervening years little evidence has been added to support this idea. The results of recent experiments designed to determine whether the lens can reduce dehydroascorbic acid to ascorbic acid were more consistent with the belief that the lens consumes this vitamin rather than produces it.[60]

Ogino and Sasamoto [61] reinvestigated this problem and conclude that ascorbic acid is synthesized by the lens. They believe that 2,3-diketogluconic acid is one of the intermediate products. The usual enzyme inhibitors, such as sodium cyanide, iodo-

56. von Euler, H.; Hellström, H.; Schlenk, F., and Günther, G.: Enzyme System of Oxidative-Reducing Mechanism in the Ocular Lens, von Graefes Arch. Ophth. **140**:116, 1939.

57. Kahan, Y. A.: Riboflavin Content in Transparent and Opaque Human Lenses and in the Urine of Patients with Cataract, Vestnik. oftal. **30**:33 (Jan.-Feb.) 1951; abstracted, Ophth. Lit. **5**:121, 1951.

58. Sobagski, C.: Respiration and Glycolysis of Chicken Lenses from the Point of View of Embryology, Acta Soc. ophth. jap. **55**:225, 1951; abstracted, Ophth. Lit. **5**:280, 1951.

59. Müller, H. K.: Studies in Lens Metabolism, Ber. Versamml. deutsch. ophth. Gesellsch. **50**:167, 184, 1934.

60. Kinsey, V. E.: Dehydroascorbic Acid-Ascorbic Acid in the Aqueous Humor of Rabbits, Am. J. Ophth. **33**:257, 1950.

61. Ogino, S., and Sasamoto, K.: Study of the Metabolism of Vitamin C in the Lens, Acta Soc. ophth. jap. **55**:47, 1951; abstracted, Ophth. Lit. **5**:288, 1951; Study of the Metabolism of Vitamin C in the Lens, Acta Soc. ophth. jap. **55**:43, 1951; abstracted, Ophth. Lit. **5**:287, 1951. Ogino, S.: Study of the Metabolism of Vitamin C in the Lens, Acta Soc. ophth. jap. **55**:49, 1951; abstracted, Ophth. Lit. **5**:288, 1951.

acetate, and phlorhizin, did not affect the synthesis. It seems unlikely that the enzymes concerned with synthesis of ascorbic acid would not be affected by any of these poisons.

Dische and Zil [62] call attention to the fact that the most striking chemical change known to occur in the lens during the the cataractous process is the decrease in amount of sulfhydryl-containing compounds. They investigated the oxidation of cysteine to cystine in lens protein during the development of senile cataract. The equilibrium between sulfhydryl and disulfide groups in the soluble protein of normal lenses was found to be such that there was present more of the reduced than of the oxidized compound, i. e., four to six times as much cysteine as cystine. In cataractous lenses the concentration of cystine increased, while that of cysteine decreased, owing to sulfhydryl oxidation; the total amount of cystine and cysteine remained the same or decreased. The ratio of cysteine to cystine in the insoluble protein albuminoid was less than in the soluble protein, and in cataractous lenses the ratio also decreased. However, the total amount of these amino acids increased, and the amount of albuminoid itself increased. Dische and Zil point out that the oxidation of sulfhydryl groups of soluble proteins precedes the increase in the concentration of albuminoid and suggest that the oxidation is one of the factors which causes precipitation of soluble proteins. This oxidation, they state, could not alone produce opacities because, as they showed, the process of oxidation is far advanced in the periphery of nuclear cataracts, where the lens is still transparent. They suggest that the reduction in the amount of glutathione present in cataractous lenses may also contribute to the opacification.

The importance of the amount of nicotinic acid in the diet in the production of "tryptophan cataract" was illustrated by feeding rats rations deficient in this vitamin, as well as low in tryptophan.[63] While no amount of nicotinic acid would prevent a cataract when animals were fed a completely tryptophan-free ration, nicotinic acid fed to animals given rations which contained insufficient tryptophan to prevent cataract did offer protection.

The water content and sodium and potassium concentrations of rabbit lenses bathed in various solutions were investigated by Harris and Gehrsitz.[64] They present evidence that the ratio of potassium to sodium, which in the normal lens is high, was reduced markedly through loss of potassium and gain of sodium ions when lenses were maintained in the absence of calcium, in the presence of iodoacetic acid and sodium fluoride, and at low temperatures. Under these conditions water was observed to accumulate subcapsularly. Less pronounced changes in the ratio of potassium to sodium resulted from elimination of magnesium from the bathing fluid, reduction in the amount of calcium to one-half that found in the aqueous humor, rupture of the capsule, replacement of glucose by xylose, fructose, or galactose, or

62. Dische, Z., and Zil, H.: Studies on the Oxidation of Cysteine to Cystine in Lens Proteins During Cataract Formation, Am. J. Ophth. **34**:104 (May, Pt. 2) 1951.

63. Pike, R. L.: Congenital Cataract in Albino Rats Fed Different Amounts of Tryptophan and Niacin, J. Nutrition **44**:191, 1951.

64. Harris, J. E., and Gehrsitz, L. B.: Significance of Changes in Potassium and Sodium Content of the Lens; A Mechanism for Lenticular Intumescence, Am. J. Ophth. **34**:131 (May, Pt. 2) 1951.

poisoning with sodium cyanide. It is suggested that the shift in cation content bears a causative relation to lenticular intumescence. However, it should not be concluded that this shift is a primary cause of cataract.

Pau [65] and Pau and associates [66] investigated the permeability of the lens capsule. They observed that capsules mounted on tubes within an hour after removal were permeable to potassium, chloride, and glucose, but impermeable to sodium, ammonium, magnesium, calcium, sulfate, and phosphate ions, and to sulfabenzamine ("marfanil"). Lenses maintained in aqueous humor, vitreous humor, or Ringer's solution increased in weight. However, lenses left in the eye up to 19 hours after death decreased in weight, but increased in weight after this time. It was postulated that 19 hours may represent the survival time of the capsular epithelium. Pau believed that the increase in weight observed post mortem was caused by the gradual decrease in the metabolism of the capsule, with the consequence that the electrolytic content approached that of the surrounding fluids. He thought that the sequence of events is as follows: First, potassium and water leave the lens, and when the metabolism of the capsule has completely ceased sodium, accompanied by water, enters the lens. The increase in weight of lenses which were removed from the eye before testing was thought to be a result of trauma. The author believes that the capsular epithelium is, in large part, responsible for the equilibrium existing between the lens and the surrounding medium. His demonstration that the equilibrium was altered by urethan, as it is also in the red blood cell, suggests that dehydrogenases may be involved in the reactions which provide energy for maintaining the equilibrium.

The uptake of various labeled ions by normal lenses and by lenses in various stages of formation of radiation cataract was determined by von Sallmann and Locke.[49] The uptake of sodium and iodine was increased in cataractous lenses, whereas that of potassium, which penetrated normal lenses rapidly, was slightly decreased. Radioactive phosphorus accumulated in normal lenses principally at the equator and in the surface layers of the cortex, presumably because of the higher metabolic rates of these parts of the lens. The difference between the amounts of phosphorus accumulating in the superficial cortical and in the deeper portions disappeared in lenses with complete radiation cataract.

The results, the authors state, do not support the theory that enhanced permeability of the lens or depressed processes of phosphorylation lead to the development of lenticular opacities produced by x-rays; they suggest, rather, that these changes accompany, and possibly influence, the progress of the opacification.

The injection of dehydroascorbic, dehydroisoascorbic, and dehydroglucoascorbic acids into rats was shown by Patterson [67] to result in cataract, caused apparently,

65. Pau, H.: Swelling of the Lens in a Physiologic Milieu, von Graefes Arch. Ophth. **151**:352, 1951; abstracted, Ophth. Lit. **5**:119, 1951; Significance of the Metabolism of the Lens Capsule, Klin. Monatsbl. Augenh. **119**:194, 1951; abstracted, Ophth. Lit. **5**:287, 1951.

66. Pau, H., and Stüttgen, G.: Problems of Physiology of the Lens, von Graefes Arch. Ophth. **151**:343, 1951; abstracted, Ophth. Lit. **5**:118, 1951. Pau, H., and Rummel, W.: Permeability Properties of the Lens Capsule, Arch. ges. Physiol. **254**:281, 1951; abstracted, Ophth. Lit. **5**:845, 1952.

67. Patterson, J. W.: Course of Diabetes and Development of Cataracts After Injecting Dehydroascorbic Acid and Related Substances, Am. J. Physiol. **165**:61, 1951.

by the resultant permanent hyperglycemia. Injection of sulfhydryl-containing compounds did not protect the animals from cataract. Patterson's results showed that a blood sugar level of 225 mg. per 100 ml. of blood for 40 days or more was required to produce a cataract.

The observation that the minimum concentration of sugar in the blood which would lead to cataract formation was the same as that which saturates the tubular resorption mechanism of the kidney led Patterson to postulate that cataract may result from a deficiency of some substance, such as amino acids or riboflavin, that is essential for lens transparency.

Not only the level of blood sugar, but also the specific configuration of the sugar, appears to be a factor in its cataractogenic action.[68] In rats fed xylose or galactose cataract developed much more quickly and in a greater proportion of cases than it did in rats treated with alloxan, despite much lower blood sugar levels.

The amino-acid composition of the proteins of ocular tissues and the relation between dietary amino-acid deficiency and cataract formation are reported in a review article by Schaeffer.[69]

IRIS AND CILIARY BODY

Carbonic anhydrase, the enzyme which catalyses the reaction $CO_2 + H_2O \rightleftarrows H_2CO_3$, was shown by Wistrand [70] to be present in uveal tissue of the rabbit in about one-seventh the concentration found in the red blood cell. This observation is of significance in connection with the theory proposed by Kinsey [6] that bicarbonate is the primary constituent of the aqueous humor that is secreted.

The presence of amine oxidase was demonstrated in the iris of the rabbit and the cat and in the nictitating membrane of the cat.[71] The relative lack of effect of arterenol on the iris can be accounted for by these results, since this enzyme destroys arterenol more readily than epinephrine.

DeRoetth [72] determined the quantity of cholinesterase present in the iris and ciliary body of rabbit eyes at various intervals after instillation of 1 drop of 0.2% diisopropyl fluorophosphate and measured the pupillary response of eyes similarly treated. He observed that cholinesterase was present in excess in the iris and ciliary body, but that only 15% of the total amount present was necessary for pupillary function. After injection of alcohol into the orbit, or after ciliary ganglionectomy, the cholinesterase activity in the iris and ciliary body was shown to decrease to 40% of normal and to remain at this level for several weeks. From these experimental procedures, which led to degeneration of the parasympathetic nerve fibers, deRoetth inferred that the remaining enzyme activity could be attributed chiefly to cholinesterase in the postsynaptic membrane.

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68. Sterling, R. E., and Day, P. L.: Blood-Sugar Levels and Cataract in Alloxan-Treated, Galactose-Fed and Xylose-Fed Weanling Rats, Proc. Soc. Exper. Biol. & Med. **78**:431, 1951.

69. Schaeffer, A. J.: Some Problems of Protein Chemistry of the Eye, Docum. ophth. **5**:403, 1951.

70. Wistrand, P. J.: Carbonic Anhydrase in the Anterior Uvea of the Rabbit, Acta physiol. scandinav. **24**:144, 1951; abstracted, Ophth. Lit. **5**:547, 1952.

71. Robinson, J.: Amine Oxidase in Iris and Nictitating Membrane, J. Physiol. **115**:39, 1951.

72. deRoetth, A., Jr.: Further Studies on Cholinesterase Activity in Ocular Tissues, Am. J. Ophth. **34**:120 (May, Pt. 2) 1951.

VITREOUS HUMOR

Several alterations in the chemical composition of the developing rabbit eye were demonstrated by Bembridge and Pirie.[73] These authors found that the protein content of the vitreous humor of the eye of the newborn rabbit was approximately 10 times that of the eye of a rabbit 3 weeks old. The protein content of the vitreous humor of the rabbit remains at this level throughout the life of the animal. They conclude that there is probably no hyaluronic acid present in the vitreous humor of the rabbit eye until about 10 days after birth.

Three fibrous components of a collagenous nature were photographed with an electron microscope.[74] The most prevalent of the three had a width of about 250 A and possibly exhibited a fine axial periodicity of about 610 A. The component present in smallest amounts apparently was collagen.

The hyaluronic acid of the vitreous humor and the polyuronic acid of the umbilical cord were thought to be identical.[75]

RETINA

The retina was found to contain an enzyme, located in the pigment epithelium and nuclear layers, which is capable of liberating two phosphoric acid radicals from adenosinephosphate.[76] Its activity did not appear to be affected by light, even in the presence of rhodopsin. The role of the enzyme in photochemistry remains to be determined.

Histochemical techniques were again employed to localize various enzymes in ocular structures. The presence of alkaline phosphatase was demonstrated in the retina, uveal tract, capsule of the lens, and, to a less extent, conjunctiva and corneal epithelium, of eyes of the mouse, guinea pig, rabbit, ox, and man.[77]

In addition to alkaline phosphatase, a specific phosphatase, 5-nucleotidase, which is considerably more active than alkaline phosphatase, was found in the retina and choroid.[78] This enzyme showed a peak activity in the physiologic range of hydrogen ion concentration, while alkaline phosphatase is relatively inactive at physiologic hydrogen ion concentrations. De Vincentiis,[79] who also observed that an alkaline phosphatase is present in the retina, was unable to demonstrate the presence of an acid phosphatase.

73. Bembridge, B. A., and Pirie, A.: Biochemical and Histological Changes in Developing Rabbit Eyes, Brit. J. Ophth. **35**:784, 1951.

74. Mateltsky, A. G.; Cerna, J., and Grigorelo, A.: A Study of the Fibrous Components of the Vitreous Body with the Electronic Microscope, Proc. Soc. Exper. Biol. & Med. **76**:857, 1951.

75. Ishiwara, T.: Biochemical Studies on Carbohydrates: C.X.L. On Mucoitin from Vitreous Humor, Tohoku J. Exper. Med. **54**:81, 1951.

76. de Benedetti, P., and Antichan, G.: Hydrolysis of Adenosine Triphosphoric Acid in the Retina and Its Biological Significance, Ann. ottal. e clin. ocul. **77**:449, 1951; abstracted, Am. J. Ophth. **35**:1012, 1952.

77. Pasquini, J., and Rabaey, M.: Histochemical Location of the Alkaline Phosphatases in the Eyes of Certain Mammals, Ann. ocul. **184**:681, 1951; abstracted, Am. J. Ophth. **34**:1771, 1951.

78. Rein, J. L.: Phosphatase Activity in the Ocular Tissues, Brit. J. Ophth. **35**:180, 1951.

79. de Vincentiis, M.: Histochemical Contribution to the Study of the Phosphatases in the Ocular Tissues, Arch. ottal. **55**:305, 1951; abstracted, Am. J. Ophth. **35**:284, 1952.

A soluble polysaccharide, tentatively identified as glycogen, was shown by a histologic staining technique to be present in the retina of the rabbit from the eighth day to the end of the third week of life.[73]

The quantity of some of the free amino acids present in bleached and unbleached retinas of frogs was estimated by paper chromatography.[80] Bleaching of the retina increased slightly the amount of amino acids present. The author also found that there are aminases and transaminases in the retina and that the quantity of amino acids is dependent upon the glycolytic and respiratory activity of this tissue.

Although much work has been done on the rates of glycolysis of retinal tissue in vitro, little is known concerning whether the glycolytic rate in vivo corresponds to that obtained in vitro. The work of de Vincentiis [81] suggests that the rates are probably similar. He determined in vitro the rate of glycolysis of the retina of various species and estimated the rate in vivo from the concentration of pyruvic and lactic acids (the products of glycolysis) found in vitreous humor.

In birds and mammals, whose rate of retinal glycolysis was high in vitro, the levels of pyruvate and lactate were found to be high in the vitreous humor in vivo. In fish and amphibians, whose rates of retinal glycolysis were low in vitro, the levels of pyruvate and lactate were found to be low in the vitreous humor in vivo. On the assumption that the vitreous humor does not metabolize, these data seemed to indicate that retinal glycolysis in vitro corresponds closely to that in vivo.

Noell [82] observed that in the rabbit and cat small doses of sodium iodoacetate injected intravenously rapidly abolished the potentials from the optic nerve and the visual cortex which result from exposure of the eye to light. Simultaneously in the rabbit the b-wave of the electroretinogram disappeared in a selective manner, and in the cat all trace of the electroretinogram was abolished. The author concludes that the energy for the generation of electrical potentials in response to illumination is furnished from aerobic glycolysis, a conclusion which is inconsistent with his observations that the electrical responses persisted in the presumed absence of aerobic conditions, i. e., under conditions of ischemia and anoxia and after the administration of carbon dioxide. These conditions, by definition, preclude the possibility of "aerobic glycolysis."

The reviewer believes that in Noell's experiments the energy was furnished from the breakdown of glucose to pyruvic and lactic acids, a process which is inhibited by iodoacetate and, as was pointed out earlier in this review, occurs either in the presence or in the absence of oxygen. It apparently was energy from this anaerobic source that produced the electrical responses observed by Noell under anoxic conditions.

Crane and Ball [83] found that the intact retina of cattle would transform carbon dioxide into dicarboxylic acids under both aerobic and anaerobic conditions and investigated the chemical mechanism by which this takes place.

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PHOTOCHEMISTRY

SECTION WRITTEN BY RUTH HUBBARD, PH.D., BIOLOGICAL LABORATORIES, HARVARD UNIVERSITY, CAMBRIDGE, MASS.

A number of contributions have been made to our knowledge of the photochemistry of vision. Rhodopsin has been synthesized in solution in a system of known components. This work was reviewed briefly from abstracts last year,[24] but it can now be described in more detail. Hubbard and Wald [84] have assembled in solution a system of four components: vitamin A, diphosphopyridine nucleotide (DPN) or cozymase, crystalline alcohol dehydrogenase from liver, and opsin (the protein moiety of rhodopsin). This mixture, in the dark, synthesizes rhodopsin in good yield. The synthesis proceeds in two steps, by the oxidation of vitamin A to retinene (vitamin-A aldehyde), coupled with the condensation of retinene with opsin to form rhodopsin. The latter is a spontaneous reaction which seems to be able to drive the oxidation of vitamin A by removing retinene as it is formed. It had previously been shown that the yield of rhodopsin in retinal homogenates is improved by supplementation with DPN and with homogenate of pigment layers. From what has been said above, the function of DPN is clear. It has now been shown that the pigment layers exert at least part of their effect by supplying more vitamin A to the alcohol dehydrogenase system. They also contain a water-soluble, heat-labile factor which increases the yield of rhodopsin, but exhibits neither opsin nor alcohol-dehydrogenase activity. The mode of action of this factor is still obscure.

Bliss [85] reports the presence in pigment layers of frog and cattle eyes of a heat-labile, nondialyzable factor—presumably a protein—which aids the synthesis of rhodopsin from the products of its bleaching, retinene and opsin. The mechanism of action of this factor and its relation to the heat-labile pigment-layer factor, mentioned above, require further investigation. Bliss [86] has also published a detailed analysis of the retinene-vitamin A equilibrium in the presence of horse-liver alcohol dehydrogenase and DPN. He found that the equilibrium constant varies linearly with the pH in the same manner as in the ethyl alcohol-acetaldehyde equilibrium. The vitamin A equilibrium, however, favors the aldehyde by a factor of about 300 as compared with the ethyl alcohol equilibrium. Bliss suggests that this may be due to a stabilization of the aldehyde group by conjugation with the five double bonds of vitamin A. He also tested the alcohol dehydrogenases from yeast and Neurospora, which proved to be incapable of catalyzing the dehydrogenation of vitamin A.

Collins [87] publishes a brief abstract describing experiments on rhodopsin synthesis from vitamin A in retinal homogenates supplemented with a variety of coenzymes and substrates. Under his conditions, aeration helps the synthesis. This

84. Hubbard, R., and Wald, G.: Mechanism of Rhodopsin Synthesis, Proc. Nat. Acad. Sc. **37**:69, 1951. Hubbard, R.: Mechanism of Rhodopsin Synthesis, Federation Proc. **10**:200, 1951.

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is not surprising, since the evidence reviewed above has shown that the oxidation of vitamin A and the reoxidation of reduced cozymase (DPN-H_2) are integral components of the reaction system.

An interesting development has come from the studies of Wald and Brown [88] on the role of sulfhydryl groups in the bleaching and synthesis of rhodopsin. They were able to show that the synthesis of rhodopsin from retinene and opsin is blocked completely by the sulfhydryl poison *p*-chloromercuribenzoate, and that the inhibition is reversible with cysteine or glutathione. Free sulfhydryl groups on opsin are therefore necessary for rhodopsin synthesis. On the contrary, in the bleaching of rhodopsin, two sulfhydryl groups are liberated per molecule of retinene. The —SH content has been measured by an adaptation of the amperometric silver titration of Kolthoff and Harris.[89] Briefly, this method allows one to determine the concentration of sulfhydryl groups by measuring the current generated by the reduction of free silver ions in a platinum-silver nitrate half-cell connected to a reference mercury-mercuric iodide half-cell through a salt bridge. The circuit is completed through a low-resistance galvanometer. Sulfhydryl compounds enter this reaction by combining with silver ions, rendering them incapable of reacting at the platinum electrode. No current, therefore, can flow until the concentration of silver is in excess of the sulfhydryl groups. In such a system, rhodopsin was titrated with silver nitrate in the dark until a current began to flow. The rhodopsin was then bleached by light, exposing sulfhydryl groups. These caused the current to decrease by combining with some of the free silver ions. As more silver was added, the current rose again. The bleaching of rhodopsin could thus be recorded as an electrical disturbance. The authors suggest that this system, however crudely, offers a model for a possible mechanism of visual excitation.

Collins, Love, and Morton [90] publish data on chemical composition of rod outer segments from cattle retinas. They were found to consist of about one-third phospholipide and 2% nucleic acid.

Peculiar effects on the visual threshold in man and on rhodopsin synthesis in the frog and toad have been reported in Japan. Hanaoka [91] shows that injection of melanophore hormone from the frog pituitary into the lymph sac of the toad increases the rate of regeneration of visual purple in vivo following light adaptation. The differential, however, is small in most experiments. He also reports an effect of melanophore hormone from cow's pituitary on the course of dark adaptation in the human eye and on the threshold of the dark-adapted eye 40 degrees from the fovea.[92] He claims that the threshold decreases reversibly, reaching a minimum

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value about 900 times below the control. From all one knows about the visual threshold of the dark-adapted periphery, it seems certain that the normal eye is approaching a limit of sensitivity imposed by the quantum nature of light. The threshold could perhaps be halved, but it is impossible to understand how a decrease of almost 3 logarithmic units can be achieved.

An extensive collation of data on visual purple and related compounds has been prepared by Krause,[93] and three general reviews have appeared in 1951. An essay by Pirenne [94] deals with some points of psychophysiologic interest. He shows, for example, that the low sensitivity of the eye to infrared radiation is necessary to achieve the states of high sensitivity of the dark-adapted eye. If the eye were more sensitive, beyond 1 μ, random heat radiation would be sufficiently intense to keep it continually light-adapted. Such a lowering of sensitivity would, of course, make vision in dim light impossible. In two short reviews, Wald [95] discusses the advances which have been made in the last two years in our understanding of the chemical processes mediating rod vision.

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Correspondence

RELATIONSHIP BETWEEN ACCOMMODATION AND CONVERGENCE

To the Editor:—I ask your permission to make a few comments on the article entitled "Relationship Between Accommodation and Convergence" by Dr. M. W. Morgan Jr., published in the June, 1952, issue of the ARCHIVES, page 745.

1. In referring to Dr. Haessler's contributions to the subject, Dr. Morgan says, "Even more startling is the claim of Haessler, who stated that positive accommodation is related to negative relative convergence."

Based on a series of tests, Dr. Haessler made such a claim and even said that from the results of his studies and graphs, "the maximum possible divergence of the optic axes of the eyes is greater when the eyes accommodate for a short distance than for a longer one" (Haessler, F. H.: Factor in Production of Divergence Increase with Near Vision, *Am. J. Ophth.* **18:** 419, 1935).

However, the conclusions of Dr. Haessler were based on an erroneous interpretation of his findings, as was shown in my article, "Does Accommodation Stimulate Divergence?" (*Am. J. Ophth.* **18:**851, 1935). Through an oversight, Dr. Haessler interpreted his findings at the near point as though the tests were made at distance, thereby overlooking the initial convergence. When this is taken into account, Dr. Haessler's findings and graphs conform to the general teachings on the relation between accommodation and convergence.

2. In determining the accommodative-convergence-accommodation ratio, Dr. Morgan uses two methods: the gradient method and the "heterophoria method." Since in both methods the degree of convergence is determined by dissociating the eyes and measuring the "phoria," either method may well be called a heterophoria method. The basic difference is that in the gradient method the tests are made at one distance and in the other method the tests are made at two distances. More suitable designations for the two methods (as I have used them in teaching this work) are the gradient method and the two-distance method.

3. In his summary the author says that there is "no relative accommodation." This statement as it stands may confuse the reader, as it is contrary not only to the teachings of the classic writers, such as Donders and Landolt, but to one's own experience. The author meant to say that there is no relative accommodation to accommodative convergence; that is, the accommodative-convergence-accommodation ratio is practically fixed and invariable. But there certainly is relative accommodation to *total* convergence. The old masters did not differentiate between the various sources of convergence innervation, and thus their findings seem at variance with the work of later investigators.

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Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

James W. Smith, M.D., *Chairman*

A. G. DeVoe, M.D., *Secretary*

Regular Meeting, Feb. 18, 1952

The entire program was devoted to a review of the "Modern Concepts of Primary Glaucoma."

In the introductory remarks, Dr. Willis S. Knighton called attention to the differences of opinion concerning the proper classification of primary glaucoma and stated that, although the classification which correlates the type of primary glaucoma with the depth of the anterior chamber had been sponsored by adequate authority, it has not met universal acceptance. He pointed out that liberal thinkers believe that there is value in each of the theories of functional versus organic obstruction and that the two systems of thought actually complement each other. He pointed out the inadequacies of the so-called provocative tests but noted that the measurement of the rate of aqueous flow may offer interesting possibilities as a diagnostic test.

Recent advances in therapy, both medical and surgical, have not been startling. At its best, surgical treatment can merely relieve the symptoms of glaucoma, without modifying the underlying cause. Whether medical therapy can so alter this basic condition remains to be seen.

Dr. Andrew deRoetth Jr. then reviewed tonographic studies on 600 eyes, pointing out the limitations and value of the procedure.

Dr. Joseph A. C. Wadsworth discussed the pathology of primary glaucoma, with particular reference to the complications occurring with trephination, iridencleisis, and cyclodiathermy.

A review of the autonomic nervous system as it relates to ocular physiology and the medical treatment of primary glaucoma was presented by Dr. P. Robb MacDonald, Philadelphia.

Dr. Harold G. Scheie, Philadelphia, reporting upon surgical management, urged conservatism. He stated that iridencleisis is now the most popular procedure for chronic simple glaucoma but that the development of cyclodiathermy and cycloelectrolysis are being watched with interest.

Dr. Algernon B. Reese then summarized the statements of the previous speakers.

James W. Smith, M.D., *Chairman*

A. G. DeVoe, M.D., *Secretary*

Regular Meeting, May 19, 1952

Sjögren's Syndrome Treated with Cortisone. Dr. Carleton Phillips.

Attention was called to the fact that this syndrome is a systemic disease, involving many parts of the body. A typical case was reported. Cortisone eye drops in an 0.5% solution was instilled hourly for the first 12 hours and thereafter at 2-hour intervals. Subjective improvement was appreciated within a few days, and within a week the objective signs of disease decreased. When oral therapy with cortisone was initiated for a concomitant arthritic disturbance, the topical use of

cortisone was discontinued. This was followed by recurrence of the ocular signs and symptoms, which were again controlled with topical administration of cortisone.

DISCUSSION

DR. SAMUEL GARTNER: Sjögren's syndrome is an obscure disease, and much of its pathogenesis and treatment has baffled us. That cortisone should be tried in such a case is logical, since the associated rheumatoid arthritis responds dramatically to it. However, as far as I can find, this is the first case of Sjögren's syndrome in which topical treatment with cortisone was followed by such improvement. What that signifies I should really like to know. It has long been thought that there is some association of the hormones with Sjögren's syndrome, because most of the patients are women and the disease usually develops at about the menopause. Attempts have been made to treat the patients with estrogens; claims have been made for improvement with such treatment, but they have not been confirmed. Further study should be made with use of cortisone eye drops in these cases and the problem further analyzed.

Tuberculosis of the Choroid. DR. ARNOLD P. PERLMAN.

A Negro aged 39 was admitted to the Veterans Administration Hospital with a history of loss of vision of three weeks' duration, presumably due to an abscess of the vitreous. During the process of enucleation, a necrotic sclera was perforated. The fluid pus was cultured for tubercle bacilli and yielded acid-fast organisms. Tuberculous meningitis subsequently developed. Recovery followed intrathecal and systemic administration of streptomycin combined with oral use of paraaminosalicylic acid. Pathological examination of the globe revealed the typical histological changes of tuberculosis.

DISCUSSION

DR. ABRAHAM S. HAFT (by invitation): The most diverse estimates of the frequency of uveal tuberculous disease are given in the literature. If the diagnosis is confined to cases in which there are clinically or histologically recognizable tubercles, the disease is rare, and with the progressive decrease in the incidence of tuberculosis in general it must become even more so. Except for acute miliary tuberculosis, ocular tuberculosis does not usually occur in the presence of active tuberculosis elsewhere, but, rather, appears in apparently normal, healthy, well-nourished persons with a healed tuberculous infection in some other organ, usually the mediastinal or hilar lymph nodes, or, more rarely, in the lungs.

The incidence of ocular tuberculosis is typical of tuberculosis in general. The disease usually affects young adults. The sexes are about equally affected. In miliary forms both eyes are usually affected, but in solitary tuberculosis one eye is usually involved. The mode of infection is hematogenous, the result of transient bacteremia, which is without systemic significance. The localization in the eye is purely fortuitous. The effect is determined by the same factors as influence the course of tuberculous infection in general; these are the virulence of the bacteria, the massiveness of the dose, and the resistance and state of allergic sensitization of the host.

The present case falls in the category of diffuse proliferative tuberculosis of the choroid. The virulence of the bacteria and the massiveness of the dose can only be conjectured. The resistance, too, is not amenable to precise measurement. There is an unequivocal body of evidence, however, that the adult Negro reacts to infection with tubercle bacilli in a manner which leaves little doubt that the Negro in general possesses a lower degree of racial resistance.

It was shown by Koch that different responses to inoculation are obtained, depending on whether or not the animal has previously been infected with tubercle bacilli. The reaction of the hypersensitive animal differs quantitatively rather than qualitatively from that of the nonhypersensitive animal. In the former, the inflammatory reaction is much more intense, usually going on to necrosis and caseation.

The present case most probably represents one of extreme hypersensitivity. The rapid clinical course and the presence of necrosis and of polymorphonuclear leucocytes in appreciable numbers in the exudate support this interpretation. Again, it has been noted that the Negro tends to acquire a higher degree of hypersensitivity to tuberculin than does the white man.

The associated meningitis is well known in the older literature. Extension may be by way either of the optic nerve or of its sheath. As has been seen in the slides, there was a large mass of tuberculous granulation tissue immediately adjacent to the nerve head. There was no involvement of the optic nerve, however, on any of the slides we studied.

The orbit was contaminated with pus, from which acid-fast bacilli were cultured. The direct communication between the subdural and subarachnoid spaces of the optic-nerve sheath and the corresponding intracranial spaces makes this route of extension to the meninges a distinct possibility in the development of the tuberculous meningitis in this case. This view is in accord with current concepts of the pathogenesis of tuberculous meningitis. Against this view are the patient's febrile course, which preceded the enucleation, the uneventful healing of the anophthalmic socket, and the short incubation period between the enucleation and the meningitis. Nine days elapsed between the enucleation and the clinical diagnosis of tuberculous meningitis as established by culture of acid-fast bacilli from the spinal fluid.

In retrospect, it is doubtful whether the diagnosis could have been made clinically at any time in the course of this patient's disease. The clinical course was notable for the complete absence of pain at any time, despite the presence of severe panophthalmitis. The histologic appearance of the sclera makes it probable that the globe would have gone on to spontaneous rupture had the process been permitted to continue. It appears from the literature that tuberculous meningitis frequently follows tuberculous panophthalmitis. It is thought that the extension to the meninges occurs by way either of the nerve itself or of its sheaths.

Radial Iridotomy in Cataract Extraction. Dr. Irving Baras and Dr. Paul C. Wetzig.

Of 988 cataract extractions performed at the New York Hospital during a five-year period, inferior radial iridotomies were performed at the time of lens extraction in 54, or 5.5%. The indications were as follows: (1) previous glaucoma surgery; (2) posterior synechae from chronic iridocyclitis; (3) corneal dystrophy; (4) central corneal opacity; (5) extracapsular extraction in which there was difficulty in removing the lens and capsular remnants; (6) updrawn pupil after lens extraction in the first eye, and (7) nondilatable pupil.

It was the belief of the authors that the performance of inferior radial iridotomy during cataract extraction in selected cases would give improved functional results and prevent the necessity for secondary operations in many instances.

DISCUSSION

Dr. John M. McLean: I have practiced and taught these techniques for 15 years and find them very satisfactory, though I do not find them as widely used as they could be, perhaps to advantage. New developments in the last two years may increase the frequency of application of these procedures in two situations. First, with the advent of adrenocortical therapy cataract extraction is being done in some cases in which the condition was usually considered inoperable before this therapy was available. It is in just that sort of a case that sphincterotomy or radial iridotomy is applicable. The other situation was recently mentioned by the younger Arruga (Arruga, A.: *Arch. Soc. oftal. hispano-am.* **11**: 1490, 1951), one with which I have had no clinical experience, but in which he performs sphincterotomy below to facilitate the introduction of Ridley plastic lenses when the pupil cannot be adequately dilated. Perhaps, if this is a procedure of the future, and I do not know whether it is or not, it may in certain cases be an indication for radial iridotomy.

Scleredema Adultorum; Ocular Manifestations. DR. THOMAS HESLIN.

A case was presented in which a clinical and laboratory diagnosis of scleredema adultorum had been made eight years previously. All symptoms subsided within 15 months except for an unusual form of chemosis, which has persisted. Puffiness of the upper and lower lids was pronounced. Bilateral superficial punctate keratitis was present in the lower halves of the corneas. The conjunctiva was notable for its solid appearing, dead-white chemosis. With the slit lamp, interlacing, coiled, discrete, tube-like channels were seen to be superficially placed. These maintained their identity during manipulation and at no time contained blood. Biopsy of the conjunctiva demonstrated stromal edema and the presence of many small endothelial-lined tubules, around which were scattered clumps of lymphocytes.

DISCUSSION

DR. GOODWIN BREININ (by invitation): In the differential diagnosis, scleredema adultorum has been confused with scleroderma, mostly because of the unfortunate similarity in sound. However, scleredema is benign and usually self-limited. whereas scleroderma results in atrophy and degeneration and has a very poor prognosis. A second disease with which scleredema may be confused is myxedema. However, in scleredema the basal metabolic rate is nearly normal, and the patient does not have the dry, scaly skin or the general manifestations. A third condition is dermatomyositis, which is a febrile disease with pain and tenderness and results in atrophy of the muscles. Cardiorenal edemas are usually self-evident.

Buschke, in 1900, stated that scleredema was a lymphatic disturbance, and in that connection our observation on the conjunctival lymphatics is interesting. Others thought that the disease was due to a collagen toxin. The most important suggestion was made by Hans Selye, author of the stress theory, who described experimental work on mice in which he applied estrogens to the skin and produced a peculiar turgid edema of the skin and subcutaneous tissue which grossly and microscopically exactly resembled this disease. Histochemical methods showed a polysaccharide in the tissue which stained metachromatically. Selye at that time thought that the disease might represent a reaction to stress in which an outpouring of estrogens or other steroids in some manner produced this edema. Duran-Reynals reported work on Macaques, in which the sex skin shows a peculiar turgid edema at estrus. Experimentally, with the use of estrogens, he was able to duplicate this swelling of the skin. The edema was caused to disappear by the use of gonadotropins and hyaluronidase. It was subsequently shown that the swelling was based on the accumulation of hyaluronic acid in the tissue. In histologic sections could be seen large vacuoles containing polysaccharides (hyaluronates) which stained metachromatically.

As a result of these studies, Dr. Heslin and I decided to see whether or not this disease could be related to a fundamental endocrine disturbance, and therefore estrogens were applied to the patient's skin locally, by rubbing, as Dr. Selye had done to mice. After a week, estradiol was injected, but to no effect. It was therefore decided that this approach would not avail anything. We decided to employ the common denominator, hyaluronidase, on the premise that the condition was due to an accumulation of hyaluronic acid in the tissue. The patient was given hyaluronidase (wydase®) in the form of drops. The results were doubtful. She thought there was some improvement, and there was a slight lessening of the punctate keratitis. Then hyaluronidase was given subconjunctivally, and it did lessen the edema. The conjunctiva, which before was firm and could not be manipulated to any extent, was made to lie flat; its large, redundant folds could be picked up readily. However, at the nasal and temporal borders of the limbus there were accumulations of lymphatic vessels, which maintained their identity at all times and could be gathered together with forceps. It was found that the hyaluronidase had only a temporary effect. This form of treatment did not accomplish anything in this case. In view of the fact that this case was a late form of the disease, it would

be worth while to pursue this approach to therapy in an early, fresh case. Cortisone was given subconjunctivally and greatly aggravated the chemosis. This result supports other clinical reports of an apparent antihyaluronidase action of cortisone.

Our purpose was threefold: (1) to describe the ocular complications of a rare systemic disease—scleredema adultorum—namely, lid edema, conjunctival chemosis, and secondary corneal trophic disturbances; (2) to describe a conjunctival lesion which might be called a type of lymphangiectasia, and (3) to describe some interesting experimental correlations which may offer help in the prognosis and treatment of the disease. I believe that the disease may be related to a systemic disturbance which produces a change in the ground substance of the mesenchyme, the alteration possibly being mediated by estrogens or adrenocortical steroids.

Bilateral Optic Neuritis Treated with Intravenous Administration of Corticotropin. Dr. Eric Smith.

A woman aged 50 with bilateral optic neuritis, whose vision was reduced to light perception in the right eye and to perception of hand movements in the left, first received oral doses of cortisone and chloromycetin for 13 days, without appreciable improvement of the vision. At that time intravenous administration of corticotropin was initiated and was maintained for the next 10 days in doses varying from 10 to 40 mg. in 1,000 cc. of 5% dextrose and water. Approximately eight hours were consumed in the daily administration of the drug. Visual improvement followed within two days, gradually improving to 20/20 — 2 in each eye.

DISCUSSION

Dr. Richard Troutman: Dr. Smith has made an exhaustive survey of the literature, parts of which he has presented here. The case reported illustrates the dramatic effect of the intravenous use of corticotropin. Under investigation at present is acthargel® (corticotropin) which promises to make treatment with this drug feasible in the outpatient department and for office patients. I believe that this preparation will be a valuable and less costly method of corticotropin treatment.

Treatment of Pseudomonas Aeruginosa Ulcer with Polymyxin B. Dr. Robert Wiggins.

The author presented three cases of a lesion diagnosed as Pseudomonas aeruginosa infection of the cornea (confirmed by cultures in two cases) in which beneficial effects followed the local use of polymyxin B administered as drops or a corneal bath, or both, in a 0.1 to 0.5% solution.

It was his opinion that at present polymyxin B is the antibiotic of choice in the treatment of Ps. aeruginosa infections of the cornea. This opinion was based on the results of experimental studies, as well as the few cases in which it has been used clinically. A suggested method of treatment might include hourly instillations and daily five-minute corneal baths with a 0.25 or 0.5% solution of polymyxin B, and the use of polymyxin ointment at night.

DISCUSSION

Dr. Ludwig von Sallmann: As Dr. Wiggins has demonstrated, the course of the corneal lesions treated by him with polymyxin B did not convey the impression of the superiority of this type of therapy over other forms of antibotic treatment and the use of sulfonamides. I am quite certain that many of us have observed similar favorable responses to other methods of local treatment. What seems to me to be of much greater importance than the observations on these patients is the fact that the results are in excellent agreement with the results of an exhaustive laboratory study carried out by Dr. Wiggins in the past. It is in the light of the results of this study that the clinical cases gained significance. Since the studies of Dr. Wiggins have not been published as yet, I think it should be men-

tioned that he tested the antibacterial activity of several promising antibiotics against a great number of strains of Ps. aeruginosa, and that he extended the study to investigate the distribution, toxicity, and penetrability of the compound on the intact and abraded cornea and the effectiveness of the treatment in experimental infections of the cornea. The results of this comprehensive piece of work pointed all in one direction, that is, that failures of local therapy in Ps.-aeruginosa infections of the cornea must be expected to occur considerably less frequently than usual when polymyxin B is selected for topical administration.

I may add here that no comparison should be made between the experimental work on Ps.-aeruginosa infections of one laboratory and the work carried out in another laboratory. The techniques of inoculation, the size of the inoculum, the drug sensitivity of the strain, its pathogenicity and invasiveness, and, last, but not least, the onset of treatment differ so greatly among published reports of various laboratories that no conclusions can be obtained from such a comparison.

I am in full agreement with Dr. Wiggins in considering polymyxin B the first choice in the treatment of infections of the cornea with Ps. aeruginosa. This opinion is not based on the clinical observations by Dr. Wiggins, but is founded on the results of the clear-cut and straightforward work with which he has enriched our knowledge of the usefulness of this drug against one of the most damaging infections of the cornea.

Bilateral Retinal Detachment Following Cataract Extraction in a Patient with Atopic Dermatitis. DR. ROBERT S. COLES.

A white woman aged 34 had had episodes of neurodermatitis since childhood, varying in intensity and usually related to emotional stress. One month after an extracapsular cataract extraction a massive retinal detachment developed. Scleral resection was unsuccessful. Six months after the initial cataract extraction, a similar extracapsular extraction was performed on the other eye. On the 18th postoperative day a massive retinal detachment was visible. No further treatment has been performed.

DISCUSSION

DR. JOSEPH LAVAL: The unhappy result obtained in Dr. Cole's case brought to my mind a similar experience I had about 15 years ago. I performed a linear cataract extraction on a man aged 25 with neurodermatitis, and shortly thereafter a retinal detachment was seen in the eye operated on. These poor results prompted me to search the literature for similar experiences. I was greatly surprised to find that of 63 reported cases in which cataract extraction was done on patients with neurodermatitis detached retina resulted in 36%. Several theories have been advanced as the cause of the retinal detachment. One is that these patients have an uncontrollable desire to scratch, and some of them have been taught by dermatologists to slap the skin. Whether they slap around the region of the eye, and this trauma causes a detachment, is debatable. Others believe there is an associated edema of the retina, which is neuroectodermal in origin, whereas the lens and the skin are ectodermal. Dr. Coles and I suggest, rather, that the vitreous, which is ectodermal, as are the lens and skin, is diseased and that therefore the diseased vitreous is responsible for the detached retina. If that assumption is correct, the operation most likely to succeed in replacing the detached retina would be a vitreous transplantation, together with a scleral resection, either partial or lamellar. I wish to emphasize that prior to cataract surgery patients with neurodermatitis should be investigated as carefully as possible for a preexisting detachment of the retina.

Complication Following Cataract Surgery: A Statistical Analysis of 1,001 Cataract Extractions. DR. ALFONSE A. CINOTTI.

Of 1,001 cases of cataract extraction, one or more complications occurred in 229. No significant difference was demonstrated in the type of conjunctival flap

used. It was believed that a higher instance of hemorrhage into the anterior chamber followed keratome than knife incision. The suturing was of the corneoscleral type, usually postplaced. There has been a shift from the use of black silk to mild chromic absorbable surgical (gut) sutures. There was little statistical difference in the complications that followed use of the various sutures. Vitreous was lost in 158 eyes, in 35% of which complications developed. Iridocyclitis was found to be the most devastating complication of cataract extraction.

DISCUSSION

DR. LOUIS J. GIRARD (by invitation): It was interesting to compare Dr. Cinotti's findings with those of Berens and Bogart (*Tr. Sect. Ophth., A. M. A.*, 1938, p. 238), who reviewed and analyzed a similar series of 1,004 cases of cataract extraction and their complications. It is particularly interesting to note that the majority of complications which follow cataract extraction are still with us in spite of the improvements in surgical techniques and the advent of antibiotics.

The complications which follow cataract extraction frequently result in partial or complete loss of vision. As causes of blindness, these complications should be analyzed critically and investigated carefully in the interest of prevention and treatment. In the time allotted, it is impossible to discuss this paper completely; however, I should like to mention one or two of the complications.

Expulsive Hemorrhage.—This devastating, but fortunately rare, complication is mentioned in most reports of a sufficiently large number of cases. Except for the Verhoeff technique of scleral puncture, no treatment has been found useful in avoiding this complication. The mechanism is not understood. The absence of the complication in this series may or may not indicate that newer techniques and management are of value in avoiding this complication.

Hemorrhage into the Anterior Chamber.—This complication is still with us, and in about the same proportion (4%) as that reported by previous investigators. Its frequency is familiar to all ophthalmic surgeons, and most surgeons, I believe, view it as not very serious. It should be noted, however, that after hyphema secondary glaucoma developed in 20% of eyes and retinal detachment in 10%. From this information, one must view any postoperative hyphema as a serious prognostic sign. The incidence is surprising in view of the availability of better sedative drugs, better anesthesia, and the antibiotics.

Iridocyclitis.—The incidence of this devastating complication is still the same as in previous reports, despite the fact that the extraction is usually done intracapsularly and despite better and less traumatic procedures and the use of antibiotics. It would seem that lens material free in the anterior chamber does materially raise the incidence of postoperative endophthalmitis phacoanaphylactica, as the incidence in extracapsular extraction is twice that in intracapsular extraction. The reports of several surgeons that this complication may be prevented by preoperative desensitization with lens antigen should have encouraged ophthalmologists to take the precaution of skin testing. However, their lack of interest in this examination has led the drug houses to take lens antigen off the market.

On the other hand, the incidence of sympathetic ophthalmitis seems to have diminished. Most investigators believe that this is due to the advent of antibiotics. This reasoning may be applied also to suppurative postoperative infections, the incidence of which has diminished considerably from that in previous reports.

On the whole, however, the problem of uvetitis is still with us. Some light may be thrown on this problem by a report of Hughes and Owens, at the Wilmer Ophthalmological Institute (*Am. J. Ophth.* **28:** 40, 1945). They analyzed their complications in relation to the presence of chronic infection and stated:

An analysis of the incidence of postoperative iridocyclitis in relation to preoperative foci of infection revealed a curious finding in the group of patients subjected to cataract extraction. In this group, the patients whose foci of infection (in teeth or sinuses) were either untreated

or inadequately treated showed essentially the same incidence of postoperative iridocyclitis as those with no demonstrable focus of infection. However, the patients whose foci of infection were adequately treated prior to the extracapsular extraction developed postoperative iridocyclitis much less frequently than either the untreated and inadequately treated group or the group with no demonstrable focus of infection.

Of 613 cases which they analyzed, no focus of infection was found in 392. The incidence of postoperative iridocyclitis in this group was 14.5%. In 126 cases foci were found but were inadequately treated. The incidence of postoperative iridocyclitis was 16.7%. In 115 cases foci were found and adequately treated. and the incidence of iridocyclitis was 4.4%.

The papers of the evening were presented by the residents.

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Combined Meeting, Dec. 17, 1951

X-RAY DIAGNOSIS OF DISEASES OF THE ORBIT

Dr. Lewis E. Etter, Pittsburgh, presented a lantern-slide demonstration of the bones of the orbit as they relate to x-ray diagnosis. Dr. Ira S. Jones and Dr. Irving Schwartz, New York, offered a similar demonstration outlining the pathological changes demonstrable in the orbit by x-rays.

RADIOTHERAPY OF DISEASES OF THE EYE

After introductory remarks by Dr. Maurice Lenz, New York, the physics of radiation therapy was reviewed by Lillian E. Jacobsen.

Clinical Application.—Dr. Clara L. Okrainetz, New York: The location of the lesion determines whether one should use high-, medium- or low-voltage x-rays, grenz-rays or beta radiation. Collaboration of the radiotherapist and the ophthalmologist is essential for accurate diagnosis and follow-up study.

Although some small hemangiomas of the eyelid in children heal spontaneously, others progress and should be treated. Complications may result from overdosage and concentration of treatment time. With x-rays, I give 300 r two or three times at weekly intervals, for a total dose of 900 to 1,200 r, using 100 kv. and half-value layer 0.85 mm. Al, the globe being completely protected by a lead shield. With radium, using a protective shield to fit the lesion, I give a maximum of 1,300 γr within two or three months.

Although resection and plastic repair are the common forms of treatment used by ophthalmologists for carcinoma of the eyelid, adequate x-ray therapy is as effective and is cosmetically preferable. I ordinarily give a total of 4,500 to 5,000 r in doses of 500 r every other day, using 100 kv. and half-value layer of 1.98 mm. Al. In the more extensive infiltrating type of tumor in which the globe has been partly involved and the orbital bone eroded, more protracted high-voltage x-ray therapy is employed. The patient is treated daily with doses of 250 r up for a total of from 5,000 to 6,000 r.

In episcleritis, satisfactory results have been obtained by screening the field and protecting the cornea, using the following factors: 1,200 r of unfiltered x-rays; 40 kv.; half-value layer, 0.4 mm. Al; target-skin distance, 15 cm.; dose, 150 r, given twice a week.

For treatment of corneal vascularization, I use a radium-D applicator, which contains 20 mg. of radium D, emitting 300 rep (the amount of beta radiation which pro-

duces the same ionization as a roentgen is called a rep—roentgen equivalent physical) at the surface, with a window 5.6 mm. in diameter. The applicator is placed in direct contact with the cornea at the limbus for a sufficient number of minutes to deliver an average dose of 900 to 3,000 rep a sitting. In the rabbit obliterative endarteritis can be produced with a dose of 6,000 rep fractionated over a three-week period. This dose is well tolerated by adjacent normal tissues of the eye. Vascularization of long standing requires intensive irradiation, whereas newly formed vessels respond to lower doses.

Pterygia and pseudopterygia respond so well that in many cases operation is unnecessary. Beta radiation is most valuable in cases of postoperative recurrence. I administer 2,400 to 3,000 rep to one field at a sitting, completing the dose in from two to three weeks. If two fields are treated, each receives 1,500 rep a sitting, and this dose is repeated in one week.

Chronic corneal ulcers with stromal infiltrates and vascularization may respond well to beta rays, and this treatment should be tried in every case in which the more conservative methods have failed. From 900 to 1,500 rep to one field at the limbus is applied at one sitting. It is necessary to repeat this treatment once, or possibly twice, up to a total of 3,000 to 4,500 rep within a month.

Vernal conjunctivitis may be successfully treated with beta irradiation of the palpebral conjunctiva, the eyeball being protected with a shield and two fields being treated at a time, 1,500 rep being administered to each field. Pronounced symptomatic improvement usually follows the first treatment. The total dose may vary from 4,500 to 7,000 rep to each field in one month.

Dr. George R. Merriam Jr.: *Beta Radiation Therapy.*—Since several hundred beta applicators are being used throughout the country, many of them by ophthalmologists, it is well to consider some of the late effects of beta radiation on the eye. A fact not generally appreciated is that the final effect of the radiation may not be fully apparent for as long as 15 to 20 years after treatment. The reported doses employed range from 120 to 4,400 mc.-min. It is impossible to state these doses accurately in reps. Reported measurements made on radon glass bulbs vary from 7 to 25 rep per millicurie-minute. An important reason for the differences in results is the variation in the thickness of the walls of the glass bulbs.

Some of the effects observed in patients treated with a radon glass bulb, in doses ranging from 250 to 2,700 mc.-min., are (1) telangiectasis of the conjunctiva; (2) keratinization of the conjunctival epithelium; (3) corneal vascularization; (4) superficial punctate keratitis; (5) corneal scarring with or without proliferation; (6) atrophy of the sclera; (7) atrophy of the ciliary body with hypotony; (8) iritis with secondary glaucoma; (9) occlusion of the angle with secondary glaucoma; (10) atrophy of the iris, and (11) radiation cataract.

The minimum dose capable of producing late changes has not been established. In the case of a malignant neoplasm, these possible late effects are relatively inconsequential as compared with the life of the patient. When benign lesions are treated, they are a real consideration.

Grenz-Ray Therapy.—My experience and that of my colleagues have confirmed the observations of Pfeiffer and others that this form of radiation is suitable for the treatment of selected superficial lesions of the eye. No harmful late effects have been observed in patients followed 14 years after treatment with doses up to 5,000 r. Patients treated with higher doses have not been observed sufficiently long to permit assessment of the final effects. Grenz rays (5 to 15 kv.) are long-wave x-rays of low penetrability, approximately 90% of which are absorbed in the first millimeter of tissue. One of the major difficulties one encounters is that of critically evaluating the results. Most of the diseases in which therapy has been employed run a variable clinical course, and it is easy for the enthusiastic therapist to accredit the result to irradiation when time and the previous medication may have been the agents responsible for the improvement.

The factors employed in grenz irradiation are 15 kv., no added filtration, 12 cm. target-skin distance, 20 ma., 1.0 to 1.5 cm. cone, and 500 r, given twice or three times a week.

The following conditions have been successfully treated:

1. Precancerous melanosis, a dose of 3,000 to 5,000 r being required.

2. Nodular episcleritis, when other forms of treatment have failed, with a total dose of 1,000 to 1,500 r.

3. Recurrent pterygia. Such therapy is not recommend for simple, uncomplicated pterygium, but is indicated in the postoperative treatment following recurrence. A maximum dose of 4,000 to 5,000 r will be sufficient.

4. Corneal vascularization. In our experience, the amount of therapy necessary to accomplish the elimination of corneal vascularization may in itself produce vascularization as a late effect. It is our belief that irradiation is not the answer to this difficult problem.

5. Phlyctenular keratoconjunctivitis. Evaluation of therapy is difficult because of the recurrent nature of the disease—1,500 r should be sufficient.

6. Bullous keratitis. Grenz-rays are employed only for the analgesic effect. There is no change in the clinical appearance of the eyes. A maximum dose of 2,500 r is usually sufficient.

7. Corneal ulcer. Resistant corneal ulcers may be benefited by 2,000 to 3,000 r of grenz rays, but the results are variable.

Epithelization of the Anterior Chamber.—We have treated 27 patients, with apparently successful results in 10, or 37%. The longest follow-up observation was three years. Two of three patients with definite cysts responded satisfactorily. Regression of the membrane was gradual, requiring 8 to 16 months to reach a final stage. In a few cases there was an annoying corneal edema after therapy, which might persist up to three years. The following factors were used: 60 kv., 20 ma., 15 cm. target-skin distance, 1.2 cm. portal, and 500 r twice a week, for a total dose of 3,000 to 5,000 r.

Lymphosarcoma.—Generalized lymphosarcoma is four times as frequent as lymphosarcoma confined to the head and neck, but the latter has a five-year survival rate of 52%, as contrasted with 26% for the generalized form. Ocular involvement may occur in the lids, lacrimal sac, conjunctiva, lacrimal gland, and orbit. The response to irradiation is excellent, and the factors employed vary according to the location and the extent of the disease. In a typical case of orbital involvement the following factors are used: 220 kv.; 0.5 mm. Cu + 1.0 mm. Al filtration (half-value layer 1.0 mm. Cu); 20 ma.; two portals—an anterior-orbital one 3.5 cm. in diameter, with a target-skin distance of 35 cm., and a temporal one 3.5 cm. in diameter, with a target-skin distance of 50 cm.—500 r being given three times a week to alternate portals for six treatments, for a total of 3,000 r $\times$ 2 (in air). A special lead face mask and conjunctival shield are used to protect the lid margins and the globe.

Retinoblastoma.—Only cases of bilateral involvement are suitable for therapy. The more involved eye is enucleated, and the fellow eye is irradiated. The factors employed are 220 kv., 0.5 mm. Cu + 1.0 mm. Al filtration (half-value layer 1.0 mm. Cu), 20 ma., 50 cm. target-skin distance, two portals—a temporal one, with a 2.5 cm. cone, and a nasal one, with a 2.0 cm. cone—400 r being given three times a week to alternate portals for 14 treatments, or 5,600 r $\times$ 2.

The results, in summary, are as follows: survivors with useful vision (20/200 or better), 33.3%; survivors without useful vision, 33.3%; nonsurvivors, 33.3%.

Other Conditions.—1. Metastatic carcinoma involving the eye or orbit can be successfully treated with radiation when indicated. The factors will vary depending upon the location of the tumor.

2. Extensive, progressive hemangiomas of the lid or conjunctiva are amenable to x-ray therapy. We have preferred to irradiate only lesions that progress in spite of adequate treatment with sclerosing solutions or applications of carbon dioxide

snow. It should be remembered, however, that approximately 98% of hemangiomas subside spontaneously. Only those that are steadily enlarging require treatment.

3. Eales's disease and diabetic retinopathy are both characterized by the presence of new-formed blood vessels on the surface of the retina and in the vitreous. X-ray therapy was formerly employed in an effort to eradicate these newly formed vessels, but its use has been discontinued, since we were unable to alter the eventual course of the disease.

DISCUSSION

DR. R. TOWNLEY PATON: It has been of great concern to me to listen to the completely discouraging reports of some of the best radiologists on the use of beta radiation in the field of ophthalmology. The misunderstanding created by this criticism should now be cleared up. As an ophthalmologist I do not pretend to know anything about radiology, but as an observer I have followed a great many patients very carefully and have noted the dramatic improvement in various types of conditions treated; many similar cases have been described here. Certain points should be clarified, however, and in order to hasten the discussion, I shall state some conclusions that I have arrived at in regard to radiation therapy.

First, no ophthalmologist should ever attempt to treat patients himself, or have the therapy under his supervision, unless he has received special training in radiotherapy. Ophthalmologists should all be warned of the serious danger and possible consequences of overtreatment or careless application. Beta-ray applicators should not become part of the office equipment of ophthalmologists. The companies distributing these applicators give one the impression that any ophthalmologist may safely treat his own patients without previous training in radiology. Much harm to the patients may result from this impression. From what I have been able to learn as a layman in this field, there is great variation in the effectiveness of these so-called standardized applicators. In the Manhattan Eye, Ear and Throat Hospital, the first applicator sent was practically useless. Fortunately, we had an efficient and skilled staff, who soon were able to obtain an effective applicator, but only after carefully checking the effectiveness of the applicator on animal eyes. An inexperienced ophthalmologist could do a great deal of harm in testing out the various types of applicators on patients' eyes, and I have known this to happen!

My second point is a warning to the radiologists who are well acquainted with the use of gamma and beta rays for certain conditions but know little, if anything, about the dangers which might result from improper handling of ophthalmological patients. The simple removal of a cinder in a highly nervous patient may be difficult even for the most skilful ophthalmologist, and treatment of ocular lesions with the various types of applicators on the market becomes a hazardous procedure for the radiotherapist unskilled in treating eyes. Constant movement of the patient's eyes and attempts at blinking make it most difficult for the radiologist and sometimes dangerous for the patient. Ulcers and erosions of the cornea have resulted, and, of course, when overtreatment occurs the results may be disastrous. The ideal set-up would be to have an ophthalmologist present whenever treatment is given.

My third point is the necessity for studying all patients with the slit lamp, both before and after treatment. Few radiologists have been trained in the use of this instrument, but in order that patients may be followed carefully, it is imperative that repeated slit-lamp examinations be made. Only by this means can the effectiveness of a treatment be observed and followed. Overtreatment is often the result of a poor follow-up system.

I believe that if these suggestions are strictly carried out there will be no criticism concerning methods of treatment.

There has been a good deal of criticism of the use of beta radiation, and frequently one hears the statement that it is too early to come to any definite conclusion concerning delayed reactions. My colleagues and I have treated ophthalmological

patients at the Manhattan Eye, Ear and Throat Hospital since 1948, and I have yet to see a radiation burn. This speaks well for the care with which our patients are treated. I have, however, seen a number of severe radiation burns in patients treated elsewhere, and in two instances the eye was completely lost as a result of overtreatment. Some radiologists claim that reactions may set in 15 or 20 years later. I wonder exactly what these reactions are. Often when episcleritis, which had previously received beta radiation, recurs, the flare-up is mistakenly attributed to overtreatment with beta radiation. I believe that the danger of delayed reactions in carefully treated eyes is slight. However, when an eye is blinded, a heroic attempt is made to save the eye; the beta radiation is given in large and too frequent doses, and a cumulative effect may be obtained. It may take several weeks before the eye quiets down, but the eye and some sight may be salvaged. I have seen two such cases, and I shall report one in illustration.

A woman aged 47 in June, 1948, had a herpetic ulcer following an infection of the upper respiratory tract. The infection spread, and for weeks she had severe keratoconjunctivitis and iritis. During the next year she consulted one ophthalmologist after another, and every known form of therapy was used, without success. Vision became reduced to hand movements, and, in final desperation, she saw two prominent ophthalmologists, both of whom thought that the eye was hopelessly gone. The patient had had a few treatments with beta radiation before the final development of the bullous-like keratitis. In a final effort to save the eye, she saw Dr. C. E. Iliff Jr., of Baltimore, who treated her during the next six months with beta rays. After only 6 gm.-sec. of beta radiation the eye showed remarkable improvement. During the next year she received a number of further treatments, these being given several months apart. Cortisone had been used topically before the beta irradiation, without much improvement. The patient continued to use cortisone during the entire period of the beta irradiation, and the sight gradually improved to 5/200. At the time of this report, the bullae have disappeared, and there is little vascularization of the scarred area; eventually, I contemplate doing a corneal transplantation.

In the second case a corneal transplantation was performed for the treatment of adherent leucoma. The vascularization threatened to spoil the operative result. (Three slides showed the dramatic improvement obtained when the blood vessels were destroyed by beta radiation.) This patient was treated by Dr. Okrainetz at the Manhattan Eye, Ear and Throat Hospital.

DR. RAMON CASTROVIEJO: I should like to discuss this presentation on radiation in ophthalmology by showing briefly a few kodachrome® transparencies illustrating cases in my own experience.

My experience closely resembles that of Dr. Merriam. In Case 1, an eye with a vascularized corneal opacity shows the results of excessive irradiation, such as telangiectasias and pronounced ischemia around the limbus.

In Case 2 there is pronounced ischemia around the limbus. Radiation was given to obliterate superficial vascularization of the cornea with the purpose of preparing the eye for keratoplasty for visual purposes. Excessive radiation rendered the eye unfit for further surgical measures to improve vision.

In Case 3 excessive radiation was given. If a corneal transplantation is performed in this eye, it will probably result in fistulization and loss of the eye.

In Case 4 a partial penetrating corneal transplantation was performed in an eye previously subjected to irradiation for corneal vascularization. Four months later the incision had not cicatrized completely, with development of a fistula requiring a total penetrating corneal transplantation to save the eye. The photograph showing the successful outcome of the second keratoplasty was taken only a few months after the operation. The final result, of course, is still uncertain.

In Case 5, one of dense vascularized corneal opacity, a keratectomy was followed by x-ray therapy, 1,500 r being given by Dr. Maurice Lenz. Since improve-

ment of vision was adequate, no further operation was necessary. If radiation is given shortly after operation, while the capillaries are radiosensitive, before they have started to invade the cornea or when they are beginning to invade it, a maximum dose of 1,500 r or less will be sufficient to inhibit the growth of the capillaries and the development of excessive fibrosis. If, then, further surgery is necessary for visual purposes, the operation can be carried out without postoperative complications. If, on the contrary, radiation is applied before operation to obliterate blood vessels already formed, a much larger dose than 1,500 r is as a rule necessary, leaving the eye unfit for further operation.

In Case 6, an eye affected with very dense and extensive corneal leucoma has been prepared by keratectomy and irradiation for final successful partial penetrating keratoplasty.

In Case 7, pterygium with a tendency to recurrence was successfully treated after operation with the minimum adequate dose of x-rays.

In case 8, malignant pterygium with several recurrences was treated by plastic repair and a buccal-mucosa implant, followed by a moderate amounts of radiation, without recurrence.

Vascularization of the cornea, in Case 9 following a partial penetrating keratoplasty, and in Case 10 following an operation for pterygium, with several recurrences, was successfully treated with ultraviolet radiation. The last two cases are reported for the first time. I have not been able to find any bibliographic reference regarding the use of ultraviolet radiation for the obliteration of corneal blood vessels. Ultraviolet radiation is effective only in obliterating superficial, and not too large, blood vessels.

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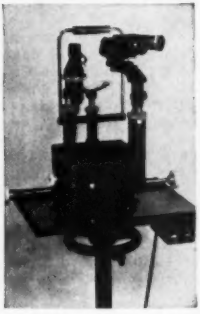

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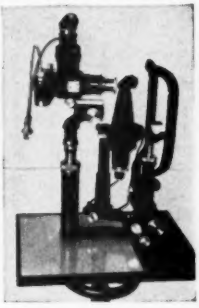

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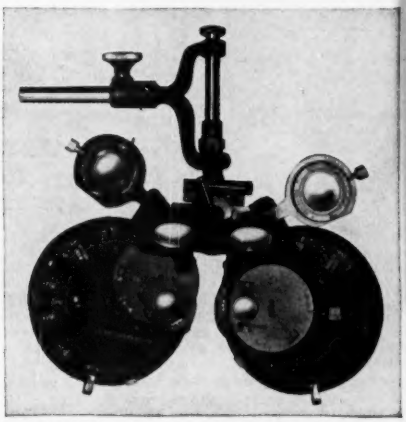

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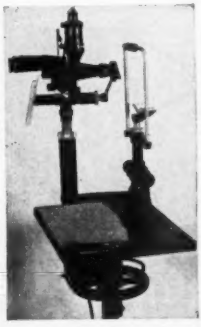

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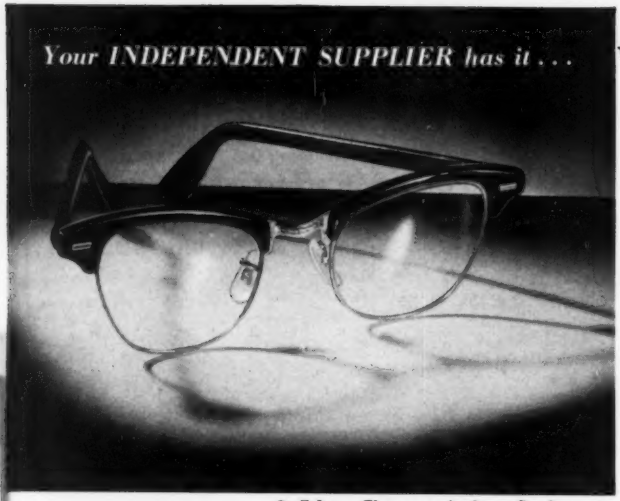

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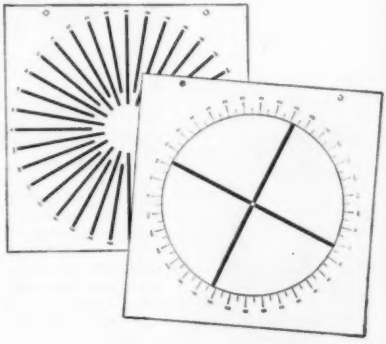

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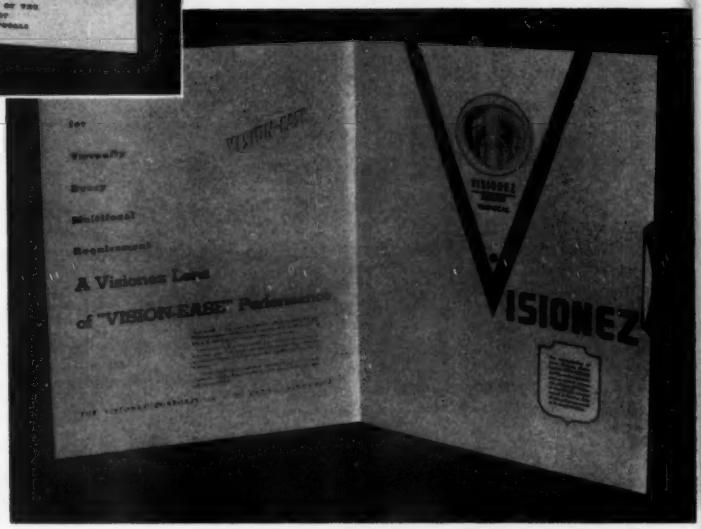

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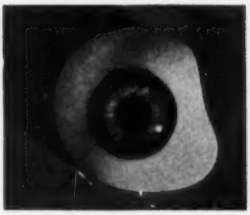

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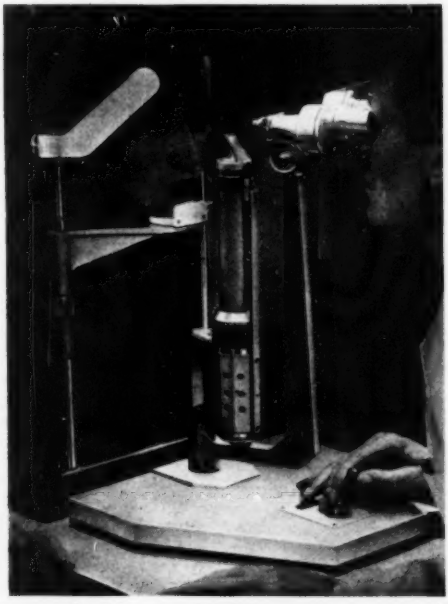

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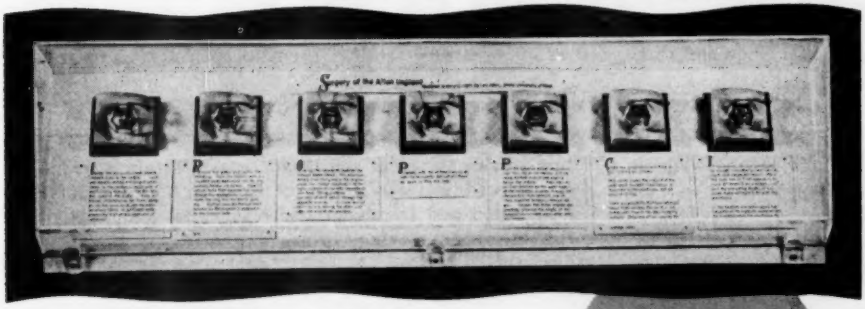

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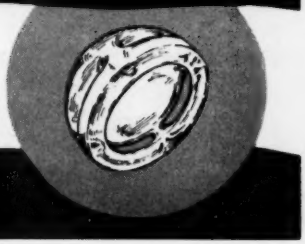

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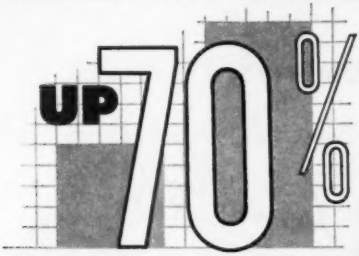

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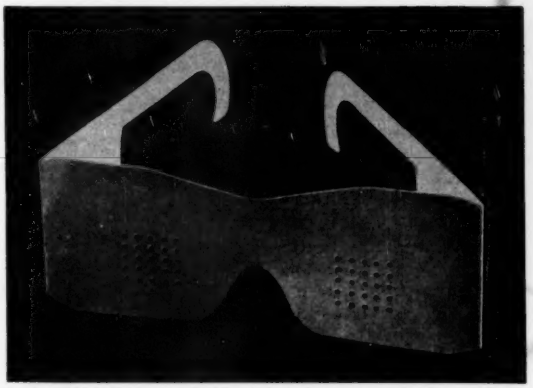

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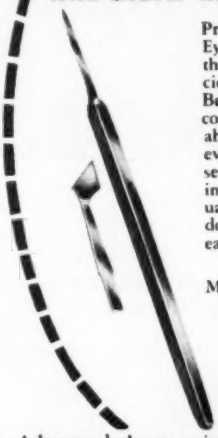

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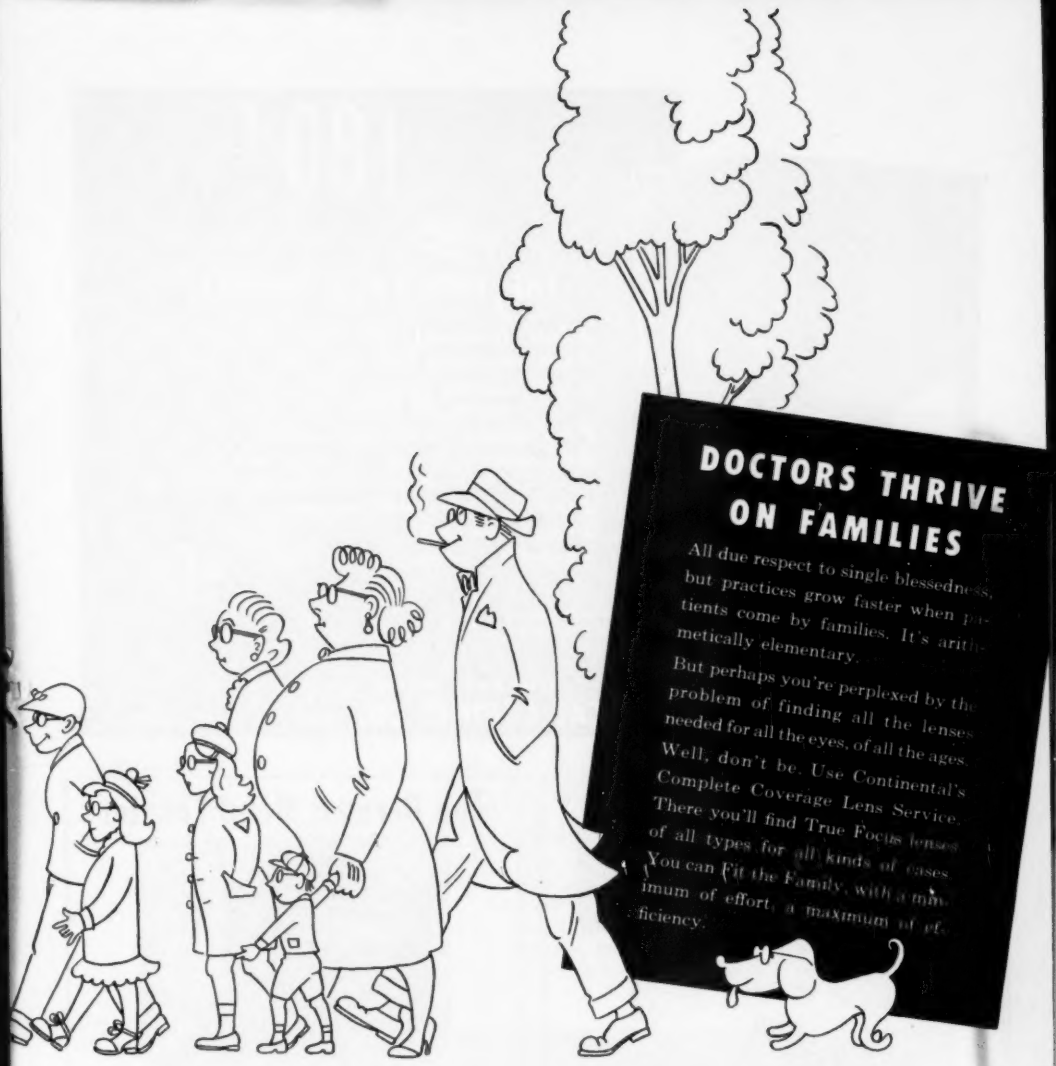
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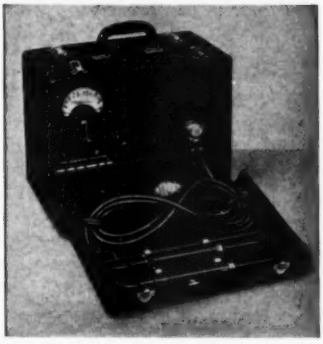

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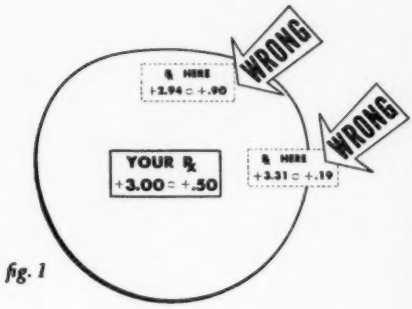

fig. 1

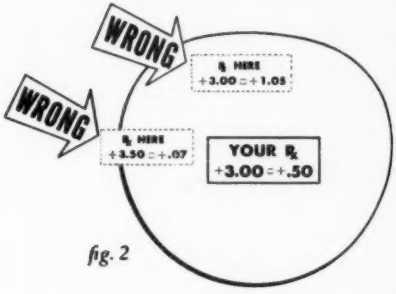

fig. 2

Highlights of the Tillyer Principle of Corrected Curve Lenses are presented once again as a timely review of the basic reasons why AO Tillyer Lenses give maximum marginal benefits.

Physically, there are limitations to designing "corrected curve" lenses with a single piece of glass.

Let's take an example:

An ordinary 6-base lens is as shown in Fig. 1. This design is as much as +.31D sphere power and +.40D cylinder power off the Rx.

By changing the curves, this lens can be corrected for sphere power error only in one meridian (Fig. 2). But, the cylinder error is now +.55D off the Rx.

By changing the curves in a different way, the lens can be corrected for cylinder error in any one meridian (Fig. 3). But, the sphere power is still −.22D off the Rx.

Here is the basic problem:

If the sphere power error is fully corrected, the cylinder error still remains. If the cylinder error is fully corrected, the sphere power error still remains.

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The AO Tillyer series of curves reduces both sphere power and cylinder errors to a negligible minimum as illustrated in Fig. 4. The AO Tillyer Corrected Curve Lens Series guarantees that your professional refraction will be protected over the entire area of the lens to the *practical limits of scientific accuracy.*

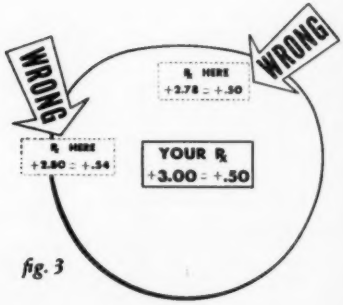

fig. 3

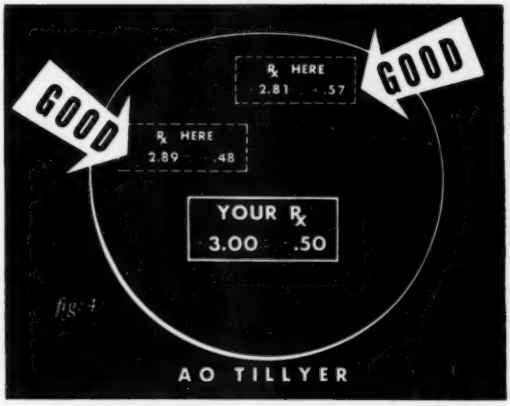

fig. 4

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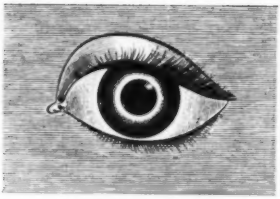

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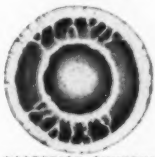
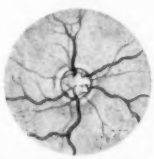
⅛% solution.
For rapid relief of congestion, itching, smarting and lacrimation.

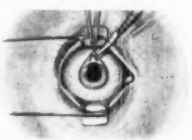
REFRACTION, FUNDUSCOPIC EXAMINATION:
2.5% solution or 1% emulsion.
For prompt and short acting mydriasis virtually free from cycloplegia.



UVEITIS, POSTERIOR SYNECHIAE:
10% solution or 10% emulsion.
For freeing recently formed posterior synechiae as well as for prevention of synechiae formation in uveitis (with atropine).



GLAUCOMA (certain cases and tests):
10% solution, 10% emulsion or 2.5% solution.
For temporary reduction of intra-ocular tension and for the provocative test for angle block.



SURGERY:
2.5% solution or 10% solution.
For short acting powerful mydriatic effect, applied 30 to 60 minutes preoperatively.

Neo-Synephrine®

HYDROCHLORIDE

Brand of phenylephrine hydrochloride

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